AIR FORCE HEALTH STUDY

An Epidemiologic Investigation of
Health Effects in Air Force Personnel
Following Exposure to Herbicides

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NATIONAL OPINION RESEARCH CENTER,
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2 May 1995

Volume V

1992 Followup Examination Results

May 1992 to May 1995

Contract Number F41624-91-C-1006
SAIC Project Number 01-0813-02-3005

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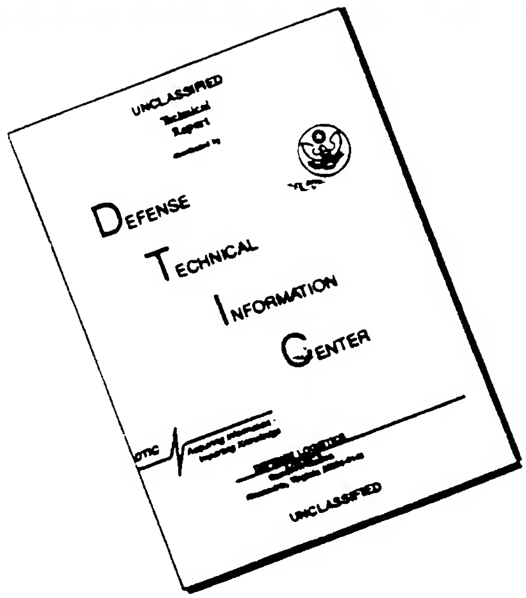

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CHAPTER 17

RENAL ASSESSMENT

INTRODUCTION

Background

In humans, there is no evidence that the kidneys are target organs for 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD, or dioxin) toxicity. Although renal excretion of phenoxy herbicides (TCDD and 2,4,5-trichlorophenoxyacetic acid [2,4,5-T]) has been well established in animals (1) and humans (2,3), more recent studies indicate that it may be of secondary importance to intestinal elimination (4,5).

Several studies have focused on the renal sequelae of chlorophenol toxicity in laboratory animals. Rats exposed to dichlorophenoxyacetic acid (2,4-D) by cutaneous application were noted to have an increase in renal weight but no histologic changes despite the development of a wasting syndrome (6). In contrast, in a study of TCDD toxicity in guinea pigs, a decrease in kidney weight was noted relative to controls, and histopathologic examination revealed focal mineralization changes in the renal parenchyma (7). Renal anomalies including hydronephrosis in mice (8-10) and hamsters (11) occurred after maternal TCDD exposure at toxic levels. In one study, these effects were limited to an aryl hydrocarbon (Ah) receptor-responsive strain (10). Because the doses of phenoxy herbicides used in these experiments were extreme by any measure of reported human exposure and because routes of administrations were not comparable, the relevance of these and other animal studies to dioxin toxicity in humans is not established.

Renal and urinary tract disease have received relatively little emphasis in morbidity studies of humans exposed to phenoxy herbicides, although an isolated case of hemorrhagic cystitis occurred in a child exposed to high concentrations of TCDD in soil (12). Acute renal failure also has been reported in cases of extreme phenoxy herbicide (though not TCDD) toxicity in man, though the mechanism appears to be secondary to rhabdomyolysis rather than to a direct nephrotoxic effect (13,14).

Epidemiologic studies of populations heavily exposed to dioxin through environmental contamination have failed to document the kidney as a target organ for TCDD toxicity (15-18), and studies of veterans potentially exposed to dioxin in Southeast Asia (SEA) have yielded similar results (19). Prior Air Force Health Study (AFHS) reports, which established the body burden of TCDD by serum levels, found no significant differences in standard indices of renal function between the Ranch Hand and Comparison cohorts (20,21). On routine microscopic urinalysis, however, 10.2 percent of those participants with high (>218 ppt) calculated initial serum dioxin levels were found to have microhematuria versus 4.9 percent of those with lower levels (25 ppt to 57 ppt) (21). Though in clinical practice such hematuria is usually of benign origin, the possibility of occult TCDD-induced renal disease is raised and will bear close scrutiny in this and subsequent examination cycles.

Summary of Previous Analyses of the Air Force Health Study

1982 Baseline Study Summary Results

The 1982 Baseline examination assessed renal disease and function by questionnaire and basic laboratory testing. Based on questionnaire information, the Ranch Hand group reported significantly more kidney disease than the Comparison group ($p=0.039$), but this finding was not substantiated by laboratory test results, even when all abnormalities in blood urea nitrogen, creatinine clearance, presence of occult blood, five or more urinary white blood cells per high-power field (WBC per HPF), and the presence of urine protein were summed. The Comparison group manifested a twofold increase in proteinuria ($p=0.055$). The distributions of creatinine clearance levels were similar for the two groups, as were the means of blood urea nitrogen, urine specific gravity, and urine WBC count. Difficulty in assessing the degree and significance of hidden noncompliance to the full 24-hour urine collection made the interpretation of the creatinine clearance test results somewhat problematic. Known noncompliance to urine collection was much more frequent ($p<0.001$) in the older participants.

The validity of the renal assessment was reinforced by the demonstrated effects of the covariates of age (born in or after 1942, born before 1942) and 2-hour postprandial glucose levels (<120 mg/dl, ≥ 120 mg/dl). Blood urea nitrogen increased with age and urine specific gravity decreased ($p<0.001$ for both), while an abnormally high postprandial glucose level indicative of diabetes was associated only with an increasing urine specific gravity, as expected.

Overall, the Baseline renal assessment suggested an excess of historical kidney disease in the Ranch Hand group not corroborated by laboratory urinalysis testing.

1985 Followup Study Summary Results

A historical assessment of kidney disease and kidney stones by a review-of-systems questionnaire showed no significant differences between the Ranch Hand and Comparison groups. Current renal function was evaluated by five laboratory variables: urine protein, urine red blood cell (RBC) counts, urine WBC counts, blood urea nitrogen, and urine specific gravity. Invasive procedures were not used.

The unadjusted analysis of proteinuria showed no group differences in contrast to the Baseline findings, which showed a marginally significant increase in proteinuria in the Comparison group ($p=0.055$). The unadjusted prevalence rates for hematuria were similar for both the Ranch Hand and Comparison groups. The approximate tenfold increase in hematuria in both groups over that observed at Baseline was most likely due to different laboratory techniques (reagent-strip testing vs. microscopic observation). Similar results were found for leukocyturia. Blood urea nitrogen levels did not vary significantly by group based on the unadjusted analysis. Overall, the blood urea nitrogen results were similar to those observed at the Baseline examination.

Unadjusted urine specific gravity levels manifested marginally significant group differences ($p=0.082$). In contrast to the Baseline values, the followup urine specific gravities were lower, a finding most likely attributable to differences in laboratory methodology (falling drop method vs. multistick procedure).

In conclusion, none of the five renal assessment variables showed a significant difference between the Ranch Hand and Comparison groups by unadjusted tests. However, in the adjusted analyses, all renal measurements except reported kidney disease revealed group-by-covariate interactions. These interactions were often complex, making it impossible to reach a firm conclusion as to the presence of a group difference.

1987 Followup Study Summary Results

Without adjustments for covariates, none of the variables of reported history of kidney disease or kidney stones, urinary protein, urinary red blood cells, urinary white blood cells, blood urea nitrogen, and urine specific gravity showed a significant difference between the two groups for the 1987 examination. In general, these findings were supported by the adjusted analyses. Examination of the group-by-covariate interactions did not yield a consistent pattern to suggest renal detriment to either the Ranch Hands or the Comparisons. Lack of a group difference in the reported history of kidney disease or kidney stones (consistent with the 1985 examination results) was in contrast with the Baseline findings, in which Ranch Hands reported significantly more disease. A nonsignificant difference in the percentage of participants with urinary protein also was inconsistent with the Baseline examination when the Comparisons had a marginally significant higher prevalence rate. In the longitudinal analysis of blood urea nitrogen, no difference in the change over time was detected.

Serum Dioxin Analysis of 1987 Followup Study Summary Results

The different sets of statistical analyses performed for the renal assessment did not indicate that an association existed between the serum dioxin levels of study participants and their 1987 examination health status. No significant associations with dioxin were observed in the longitudinal analyses of blood urea nitrogen. For some adjusted analyses, diabetic class was a significant covariate in the model. Because dioxin may influence diabetic status, ancillary models without diabetic class also were examined. For the most part, deletion of diabetic class from an adjusted model had no appreciable effect on the outcome of the analysis.

Parameters for the Renal Assessment

Dependent Variables

The Renal Assessment was based on laboratory data collected at the 1992 physical examination, as well as on a verified history of kidney disease, as reported by the participant and subsequently verified by a medical records review.

Medical Records Data

In the self-administered family and personal history questionnaire, each study participant was asked whether he had ever experienced kidney trouble or kidney stones or had recurrent occurrences of kidney infections in the years prior to the 1992 physical examination. This information was subsequently verified and combined with data from previous examinations and from the physical examination. A composite variable, kidney disease, was constructed by assigning "yes" to any participant who was verified to have had at least one of the following conditions: kidney trouble, kidney stones, or kidney infections.

Participants with a pre-SEA history of one of these conditions were excluded from the analysis. No other participants were excluded for medical reasons from the analysis of this variable.

Physical Examination Data

Kidney stones (present, absent), as determined by the kidney, urethra, and bladder (KUB) x ray, were analyzed.

Laboratory Examination Data

Five renal variables were quantified by general laboratory procedures to assess nonspecific renal system function. Urinary protein and urine specific gravity were determined by accepted dipstick methods using a Clinitek 200®. Hematuria and leukocyturia were measured by high-powered microscopic examination. Serum creatinine was assayed using Baxter/Dade Paramax® equipment.

Urinary protein (absent, present), hematuria ($\leq$ 2 urinary red blood cells per high-powered field [RBC per HPF], $>$ 2 RBC per HPF), and leukocyturia ($\leq$2 urinary WBC per HPF, $>$2 WBC per HPF) were analyzed as dichotomous variables. Serum creatinine (mg/dl) and urine specific gravity were analyzed as continuous variables.

The Scripps Clinic and Research Foundation (SCRF) normal range for serum creatinine was 0.5-1.2 mg/dl, and 1.005-1.030 mg/dl for urine specific gravity. However, statistical analyses were only performed for these variables in the continuous form.

No participants were excluded for medical reasons from the analysis of these variables.

Covariates

The effects of the four covariates age, race, military occupation, and diabetic class were examined in adjusted statistical analyses of the renal data. Diabetic class was defined as diabetic (verified history of diabetes or $\geq$200 mg/dl 2-hour postprandial glucose), impaired (140 mg/dl $\leq$ 2-hour postprandial glucose $<$200 mg/dl), and normal ($<$140 mg/dl 2-hour postprandial glucose). Age was used in its continuous form for modeling purposes for all dependent variables. Age was dichotomized for clarity of presentation (e.g., interaction summaries).

Statistical Methods

Chapter 7, Statistical Methods, describes the basic statistical methods used throughout this report. Table 17-1 summarizes the statistical analyses performed for the Renal Assessment. The first part of this table describes the dependent variables and identifies the candidate covariates and the statistical methods. The second part of the table further describes the candidate covariates. Abbreviations used in the body of the table are defined at the end of the table. Table 17-2 provides the number of participants excluded for a pre-SEA history of kidney disease and the number of participants with missing dependent variable or diabetic class status data.

Analyses of data collected at the 1987 followup study indicated that dioxin was associated with military occupation. In general, enlisted personnel had higher levels of dioxin than officers, with enlisted groundcrew having higher levels than enlisted flyers. Consequently, adjustment for military occupation in statistical models using dioxin as a measure of exposure may improperly mask an actual dioxin effect. However, occupation also can be a surrogate for socioeconomic effects. Failure to adjust for occupation could overlook important risk factors related to lifestyle. If occupation was found to be significantly associated with a dependent variable in the 1992 followup analyses and was retained in the final statistical models using dioxin as a measure of exposure, the dioxin effect was evaluated in the context of two models. Analyses were performed with and without occupation in the final models to investigate whether conclusions regarding the association between the health endpoint and dioxin differed.

Diabetes also exhibited a significant positive association with dioxin in the serum dioxin analysis of the 1987 followup data. The results of similar diabetic analyses for the 1992 followup are discussed in Chapter 18, Endocrine Assessment. Consequently, clinical endpoints in the Renal Assessment may be related to dioxin due to the association between dioxin and diabetes. To investigate this possibility, the dioxin effect was evaluated in the context of two models whenever diabetic class was retained in the final model. Analyses again were performed with and without diabetic class in the model to investigate whether conclusions regarding the association between the health endpoint and dioxin differed.

The results of the analyses without occupation and diabetic class in the final adjusted model are presented in Appendix M-3 and are only discussed in the text if the level of significance differs from the original final adjusted model (significant versus nonsignificant).

Longitudinal Analysis

Longitudinal analyses were conducted on four laboratory variables (urinary red blood cell count, urinary protein, urinary white blood cell count, and urine specific gravity) to evaluate the changes between previous examinations and the 1992 followup examination. The longitudinal analyses for urinary protein investigated differences between the 1982 examination and the 1992 examination because the same measurement method was used at each examination. By contrast, the longitudinal analyses for urinary red blood cell count and urine specific gravity assessed changes between the 1985 examination and the 1992 examination because the 1982 examination employed a different measurement method than

Table 17-1.
Statistical Analyses for the Renal Assessment

Dependent Variables

Variable (Units)	Data Source	Data Form	Cutpoints	Candidate Covariates	Statistical Analysis
Kidney Disease	MR-V	D	Yes No	AGE,RACE,OCC, DIAB	U:LR,CS A:LR
Kidney Stones from KUB X-Ray	PE	D	Present Absent	AGE,RACE,OCC, DIAB	U:LR,CS A:LR
Urinary Protein	LAB	D	Present Absent	AGE,RACE,OCC, DIAB	U:LR,CS A:LR L:LR
Urinary Red Blood Cell Count (RBC per HPF)	LAB	D	Abnormal: >2 Normal: ≤ 2	AGE,RACE,OCC, DIAB	U:LR,CS A:LR L:LR
Urinary White Blood Cell Count (WBC per HPF)	LAB	D	Abnormal: >2 Normal: ≤ 2	AGE,RACE,OCC, DIAB	U:LR,CS A:LR L:LR
Serum Creatinine (mg/dl)	LAB	C	--	AGE,RACE,OCC, DIAB	U:GLM,TT A:GLM
Urine Specific Gravity	LAB	C	--	AGE,RACE,OCC, DIAB	U:GLM,TT A:GLM L:GLM

Covariates

Variable (Abbreviation)	Data Source	Data Form	Cutpoints
Age (AGE)	MIL	D/C	Born $\geq$ 1942 Born $<$ 1942
Race (RACE)	MIL	D	Black Non-Black
Occupation (OCC)	MIL	D	Officer Enlisted Flyer Enlisted Groundcrew
Diabetic Class (DIAB)	LAB and MR-V	D	Diabetic: past history or $\geq$200 mg/dl 2-hr. postprandial glucose Impaired: $\geq$140$-\leq$200 mg/dl 2-hr. postprandial glucose Normal: $<$140 mg/dl 2-hr. postprandial glucose

Table 17-1. (Continued)
Statistical Analyses for the Renal Assessment

Abbreviations

Data Source:	LAB	=	1992 laboratory results
	MIL	=	Air Force military records
	MR-V	=	Medical records (verified)
	PE	=	1992 physical examination
Data Form:	C	=	Continuous analysis only
	D	=	Discrete analysis only
	D/C	=	Appropriate form for analysis (either discrete or continuous)
Statistical Analyses:	U	=	Unadjusted analyses
	A	=	Adjusted analyses
	L	=	Longitudinal analyses
Statistical Methods:	CS	=	Continuity-adjusted chi-square statistic
	GLM	=	General linear models analysis
	LR	=	Logistic regression analysis
	TT	=	Two-sample t-test

Table 17-2.
Number of Participants with Missing Data for, or Excluded from, the Renal Assessment

Variable	Variable Use	Group		Dioxin (Ranch Hands Only)		Categorized Dioxin	
		Ranch Hand	Comparison	Initial	Current	Ranch Hand	Comparison
Urinary Protein	DEP	2	2	2	2	2	1
Urinary Red Blood Cell Count	DEP	2	2	2	2	2	1
Urinary White Blood Cell Count	DEP	2	2	2	2	2	1
Serum Creatinine	DEP	0	1	0	0	0	0
Urine Specific Gravity	DEP	2	2	2	2	2	1
Diabetic Class	COV	1	2	0	1	1	1
Pre-SEA Kidney Disease	EXC	21	30	11	21	21	22

Abbreviations: DEP = Dependent variable (missing data).
COV = Covariate (missing data).
EXC = Exclusion.

Note: 952 Ranch Hands and 1,281 Comparisons;
520 Ranch Hands for initial dioxin; 894 Ranch Hands for current dioxin;
894 Ranch Hands and 1,063 Comparisons for categorized dioxin.

One Ranch Hand missing total lipids for current dioxin.

the procedure used at subsequent examinations (reagent strip testing in 1982 vs. microscopic observation for urinary red blood cells; falling drop in 1982 vs. multistick for urine specific gravity).

The longitudinal analyses for urinary white blood cell count investigated differences between the 1985 and 1992 examinations because, even though all the examinations employed the same measurement method (microscopic observation), the cutpoint for defining an abnormality changed between the 1982 examination and subsequent examinations (>4 urinary WBC per HPF in 1982 vs. >2 urinary WBC per HPF in 1985, 1987, and 1992). See Chapter 7, Statistical Methods, for a further discussion of methods used in the longitudinal analysis.

RESULTS

Dependent Variable-Covariate Associations

Unadjusted covariate tests of association were done to examine the relationships between the dependent variables and the candidate covariates—age, race, occupation, and diabetic class. Analyses were performed on the combined Ranch Hand and Comparison group cohorts. Associations with a p-value less than 0.10 are discussed below.

Kidney disease was significantly associated with age and diabetic class (Appendix Table M-1-1: $p=0.001$ and $p<0.001$ respectively). Older participants were more likely to have a verified history of kidney disease than younger participants (18.8% of men born before 1942 vs. 13.2% of men born in or after 1942), and diabetics had a higher rate of kidney disease than subjects with normal and impaired glucose levels. The percentages of AFHS participants with a verified history of kidney disease in the normal, impaired, and diabetic categories were 14.7, 17.4, and 24.0 percent respectively.

The only covariate significantly associated with kidney stones was age ($p=0.023$), with older participants having a higher rate of occurrence than younger participants (3.6% vs. 1.9%).

The only covariate significantly associated with urinary protein was diabetic class ($p<0.001$). Diabetics were much more likely to have urinary protein abnormalities (13.9%) than were subjects with impaired glucose levels (4.8%) and subjects with normal glucose levels (2.7%).

Urinary red blood cell count was significantly associated with occupation ($p=0.018$) and race ($p=0.007$). The percentages of abnormalities for officers, enlisted flyers, and enlisted groundcrew were 1.7 percent, 2.2 percent, and 3.8 percent respectively. Blacks were more than twice as likely as non-Blacks to have urinary red blood cell count abnormalities (6.9% vs. 2.5%).

Covariate analyses for urinary white blood cell count were significant for occupation ($p=0.031$) and diabetic class ($p=0.003$). For occupation, enlisted flyers had the highest percentage of urinary white blood cell abnormalities (4.7%) followed by enlisted groundcrew

(3.1%) and officers (2.0%). For diabetic class, diabetics were more than twice as likely to have urinary white blood cell abnormalities than either subjects with impaired glucose levels or those with normal levels (5.9% of diabetics vs. 2.8% of impaired and 2.4% of normal).

Covariate analyses for serum creatinine revealed a significant association with age ($p=0.004$) and race ($p<0.001$), and a marginally significant association with diabetic class ($p=0.081$). Age was positively correlated with serum creatinine, and Blacks had a higher mean level of serum creatinine than non-Blacks (1.0513 mg/dl vs. 0.9692 mg/dl). Of the diabetic class categories, diabetics had the lowest mean level of serum creatinine (0.9584 mg/dl) while subjects with impaired glucose levels had the highest mean level (0.9877 mg/dl). Normal subjects had a mean level of serum creatinine of 0.9750 mg/dl.

Urine specific gravity was significantly associated with occupation ($p<0.001$) and diabetic class ($p=0.002$) and marginally associated with age ($p=0.081$) and race ($p=0.069$) in the covariate tests of association. Of the occupational categories, enlisted groundcrew had the highest mean urine specific gravity (1.0196), while the mean for both enlisted flyers and officers was 1.0182. For diabetic class, the means were 1.0186, 1.0194, and 1.0198 for the normal, impaired, and diabetic categories respectively. Age was negatively correlated with urine specific gravity ($r=-0.037$, $p=0.081$). Blacks had a higher mean urine specific gravity than non-Blacks (1.0198 vs. 1.0188).

In summary, the covariate tests of association found that older participants were more likely than younger participants to have a verified history of kidney disease, evidence at the physical examination of kidney stones, higher serum creatinine, and a lower mean urine specific gravity. Racial differences showed that Blacks were more likely than non-Blacks to have urinary red blood cell count abnormalities, a higher serum creatinine level, and a higher urine specific gravity. Of the occupational categories, enlisted groundcrew had the highest prevalence of urinary red blood cells and the highest levels of urine specific gravity, while enlisted flyers had the highest prevalence of urinary white blood cells. Associations with the diabetic class covariate found that, as expected, diabetics were more likely than nondiabetics to have a history of kidney disease, urinary protein, urinary white blood cells, a lower serum creatinine level, and a higher urine specific gravity.

Exposure Analysis

The following section presents the results of the statistical analyses of the dependent variables shown in Table 17-1. Dependent variables are grouped into three sections: those derived and verified from a review of medical records, data obtained during the 1992 physical examination, and data derived from the laboratory portion of the 1992 followup examination.

Unadjusted and adjusted analyses of six models are presented for each variable. Model 1 examines the relationship between the dependent variable and group (Ranch Hand or Comparison). Model 2 explores the relationship between the dependent variable and an extrapolated initial dioxin measure for Ranch Hands who had a 1987 dioxin measurement greater than 10 ppt. If a participant did not have a 1987 dioxin level, a 1992 level was used. A statistical adjustment for the percent of body fat at the participant's time of duty in SEA

and the change in the percent of body fat from the time of duty in SEA to the date of the blood draw for dioxin is included in this model to account for body-fat-related differences in elimination rate (22). Model 3 dichotomizes the Ranch Hands in Model 2 based on their initial dioxin measures; these two categories of Ranch Hands are referred to as the "low Ranch Hand" category and the "high Ranch Hand" category. These participants are added to Ranch Hands and Comparisons with current serum dioxin levels (1987, if available; 1992, if the 1987 level was not available) at or below 10 ppt to create a total of four categories. Ranch Hands with current serum dioxin levels at or below 10 ppt are referred to as the "background Ranch Hand" category. The relationship between the dependent variable in each of the three Ranch Hand categories and the dependent variable in the "Comparison" category is examined. A fourth contrast, exploring the relationship of the dependent variable in the low Ranch Hand category and the high Ranch Hand category combined, also is conducted. This combination is referred to in the text and tables as the "low plus high Ranch Hand" category. As in Model 2, a statistical adjustment is made for the percent of body fat at the participant's time of duty in SEA and the change in the percent of body fat from the time of duty in SEA to the date of the blood draw for dioxin.

Models 4, 5, and 6 examine the relationship between the dependent variable and 1987 dioxin levels in all Ranch Hands with a dioxin measurement. If a participant did not have a 1987 dioxin measurement, a 1992 measurement was utilized in determining the current dioxin level. The measure of dioxin in Model 4 is lipid-adjusted, whereas whole-weight dioxin is used in Models 5 and 6. Model 6 differs from Model 5 in that a statistical adjustment for total lipids is included in Model 6. Further details on dioxin and the modeling strategy are found in Chapters 2 and 7 respectively.

Results of investigations for group-by-covariate and dioxin-by-covariate interactions are referenced in the text, and tabular results are presented in Appendix M-2. As described previously, additional analyses were performed when occupation or diabetic class was retained in the final models for Models 2 through 6. Results excluding occupation and diabetic class from these models are tabled in Appendix M-3. Results from analyses excluding occupation and diabetic class are discussed in the text only if a meaningful change occurred (that is, changes between significant results, marginally significant results, and nonsignificant results).

Verified Medical Records Variable

Kidney Disease

The results from the Model 1 analysis did not detect a significant difference in the history of kidney disease between Ranch Hands and Comparisons (Table 17-3(a,b): $p>0.22$ for all contrasts). The adjusted analysis accounted for diabetic class and the age-by-occupation interaction.

Similarly, Models 2 and 3 did not show kidney disease to be significantly associated with initial dioxin or categorized dioxin (Table 17-3(c-f): $p>0.56$ for all analyses). For Model 2, the final adjusted model was the same as the unadjusted model; however, the adjusted analysis of Model 3 contained the covariates age, occupation, and diabetic class.

Table 17-3.
Analysis of Kidney Disease

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Yes**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***931***	***17.0***	***1.08 (0.86,1.36)***	***0.545***
	Comparison	***1,251***	***15.9***		
Officer	Ranch Hand	358	17.3	1.28 (0.88,1.87)	0.225
	Comparison	485	14.0		
Enlisted Flyer	Ranch Hand	158	16.5	1.12 (0.63,1.98)	0.818
	Comparison	200	15.0		
Enlisted Groundcrew	Ranch Hand	415	16.9	0.93 (0.67,1.31)	0.754
	Comparison	566	17.8		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***1.08 (0.86,1.36)***	***0.526***	DIAB (p=0.025) OCC*AGE (p=0.034)
Officer	1.25 (0.85,1.83)	0.256	
Enlisted Flyer	1.13 (0.64,2.00)	0.681	
Enlisted Groundcrew	0.95 (0.68,1.33)	0.752	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 17-3. (Continued)
Analysis of Kidney Disease

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	170	17.1	0.97 (0.81,1.15)	0.717
Medium	170	17.1		
High	169	17.8		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[a]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
509	0.97 (0.81,1.15)	0.717	

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 17-3. (Continued)
Analysis of Kidney Disease

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,041	16.0		
Background RH	364	16.2	1.07 (0.77,1.48)	0.690
Low RH	253	17.0	1.04 (0.72,1.51)	0.830
High RH	256	17.6	1.08 (0.75,1.55)	0.694
Low plus High RH	509	17.3	1.06 (0.80,1.41)	0.695

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,040			AGE ($p<0.001$) OCC ($p=0.016$) DIAB ($p=0.030$)
Background RH	363	1.11 (0.79,1.55)	0.560	
Low RH	253	1.01 (0.69,1.47)	0.960	
High RH	256	1.06 (0.72,1.54)	0.773	
Low plus High RH	509	1.03 (0.77,1.38)	0.828	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 17-3. (Continued)
Analysis of Kidney Disease

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Yes/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	15.0 (286)	18.3 (295)	17.1 (292)	1.02 (0.90,1.15)	0.729
5	14.1 (291)	19.2 (291)	17.2 (291)	1.02 (0.92,1.14)	0.685
6[c]	14.1 (291)	19.2 (291)	17.2 (291)	1.01 (0.90,1.13)	0.918

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	873	1.07 (0.94,1.21)	0.313	AGE*RACE (p=0.032)
5	873	1.06 (0.95,1.18)	0.329	AGE*RACE (p=0.033)
6[d]	873	1.05 (0.93,1.18)	0.480	AGE*RACE (p=0.034)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

For Models 4 through 6, no significant association between history of kidney disease and current dioxin was found in the unadjusted and adjusted analyses (Table 17-3(g,h): $p>0.31$ for all analyses). Each of the adjusted analyses for Models 4 through 6 accounted for the age-by-race interaction.

Physical Examination Variable

Kidney Stones

As shown in Table 17-4(a,b), the unadjusted and adjusted analyses for Model 1 did not reveal a significant association between kidney stones and group ($p>0.46$ for all contrasts). The final model in the adjusted analysis for Model 1 contained the covariate age.

Examination of the unadjusted results for Model 2 revealed a significant inverse relationship between initial dioxin and kidney stones (Table 17-4(c): $p=0.016$, Est. RR=0.58, 95% C.I.=[0.36, 0.94]). The percentages of participants with kidney stones in the low, medium, and high initial dioxin categories were 5.2, 2.9, and 1.7 percent respectively.

The adjusted analysis for Model 2 detected a significant initial dioxin-by-diabetic class interaction (Table 17-4(d): $p=0.016$). Appendix Table M-2-1 presents stratified results to examine this interaction. Age also was a significant covariate in the final model. After deleting the initial dioxin-by-diabetic class interaction from the final model, a marginally significant inverse relationship between initial dioxin and kidney stones was detected (Table 17-4(d): $p=0.069$, Adj. RR=0.65, 95% C.I.=[0.39, 1.07]).

The unadjusted and adjusted analyses of Model 3 did not uncover a significant association between kidney stones and categorized dioxin (Table 17-4(e,f): $p>0.24$ for unadjusted and adjusted results). Although the prevalence rates in the three Ranch Hand categories did not differ significantly from the Comparison group prevalence rate, the percentage of abnormalities decreased from the low Ranch Hand category to the high Ranch Hand category, which was consistent with the results of Model 2. The lack of significant differences between the Ranch Hand categories and Comparison group is consistent with the results of Model 1. Age was the only significant covariate in the adjusted analysis of Model 3.

As presented in Table 17-4(g,h), none of the analyses for Models 4 through 6 uncovered a significant association between kidney stones and current dioxin ($p>0.51$ for all analyses). Each of the adjusted analyses for Models 4 through 6 accounted for the covariate age.

Table 17-4.
Analysis of Kidney Stones

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Present**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***952***	***3.0***	***1.12 (0.68,1.84)***	***0.755***
	Comparison	***1,281***	***2.7***		
Officer	Ranch Hand	367	3.3	0.91 (0.43,1.91)	0.949
	Comparison	502	3.6		
Enlisted Flyer	Ranch Hand	162	3.7	1.26 (0.40,3.99)	0.918
	Comparison	203	3.0		
Enlisted Groundcrew	Ranch Hand	423	2.6	1.37 (0.59,3.19)	0.605
	Comparison	576	1.9		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***1.11 (0.67,1.83)***	***0.684***	AGE (p=0.004)
Officer	0.90 (0.43,1.89)	0.777	
Enlisted Flyer	1.25 (0.39,3.95)	0.709	
Enlisted Groundcrew	1.37 (0.59,3.20)	0.462	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 17-4. (Continued)
Analysis of Kidney Stones

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Present	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	174	5.2	0.58 (0.36,0.94)	0.016
Medium	173	2.9		
High	173	1.7		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
520	0.65 (0.39,1.07)**	0.069**	INIT*DIAB (p=0.016) AGE (p=0.016)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Log_2 (initial dioxin)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table M-2-1 for further analysis of this interaction.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.
INIT = Log_2 (initial dioxin).

Table 17-4. (Continued)
Analysis of Kidney Stones

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Present	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,063	2.5		
Background RH	374	2.7	1.02 (0.49,2.14)	0.957
Low RH	260	3.8	1.55 (0.74,3.25)	0.246
High RH	260	2.7	1.09 (0.47,2.54)	0.839
Low plus High RH	520	3.3	1.32 (0.71,2.46)	0.377

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,063			AGE (p=0.020)
Background RH	374	0.97 (0.46,2.03)	0.929	
Low RH	260	1.49 (0.71,3.14)	0.291	
High RH	260	1.23 (0.53,2.89)	0.630	
Low plus High RH	520	1.37 (0.74,2.56)	0.316	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 17-4. (Continued)
Analysis of Kidney Stones

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Present/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	2.0 (295)	5.0 (300)	2.0 (299)	0.91 (0.70,1.20)	0.510
5	1.7 (300)	5.1 (297)	2.4 (297)	0.94 (0.75,1.18)	0.613
6[c]	1.7 (299)	5.1 (297)	2.4 (297)	0.94 (0.74,1.20)	0.623

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	894	0.96 (0.72,1.27)	0.766	AGE (p=0.057)
5	894	0.98 (0.77,1.24)	0.850	AGE (p=0.053)
6[d]	893	0.98 (0.76,1.27)	0.898	AGE (p=0.052)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for $\log_2$ total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for $\log_2$ total lipids.

[d] Adjusted for $\log_2$ total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Laboratory Examination Variables

Urinary Protein

Table 17-5(a,b) demonstrates that group differences in the presence of urinary protein were not statistically significant ($p > 0.20$ for all analyses). Covariate adjustment for the Model 1 analysis accounted for age, occupation, and diabetic class.

Analyses of Models 2 and 3 did not show initial dioxin or categorized dioxin to be significantly associated with urinary protein (Table 17-5(c-f): $p > 0.15$ for all analyses). The adjusted analysis for Model 2 accounted for diabetic class, while the adjusted analysis for Model 3 contained the covariates age, occupation, and diabetic class.

Table 17-5(g,h) displays results for the current dioxin analysis of urinary protein. No statistically significant results were found in any of the unadjusted analyses for Models 4 through 6 ($p > 0.36$ for each unadjusted analysis). The adjusted analyses for Models 4, 5, and 6 each had a significant current dioxin-by-diabetic class interaction (Table 17-5(h): $p=0.004$, $p=0.012$, and $p=0.011$ respectively). Appendix Table M-2-2 presents results stratified by each level of diabetic class. The relationship between dioxin and diabetes is discussed in Chapter 18, Endocrine Assessment. The age-by-race interaction was also significant in the adjusted analyses of Models 4 through 6. Current dioxin was not found to be significantly associated with urinary protein after removing the current dioxin-by-diabetic class interaction from the final adjusted models (Table 17-5(h): $p > 0.53$ for all analyses).

Urinary Red Blood Cell Count

The percentage of participants with abnormal urinary red blood cell counts did not differ significantly between the Ranch Hand and Comparison groups in the Model 1 analyses (Table 17-6(a,b): $p > 0.17$ for each analysis). The adjusted analysis accounted for age, race, and occupation.

No significant association was detected between initial dioxin and urinary red blood cell count in the unadjusted and adjusted analyses of Model 2 (Table 17-6(c-d): $p > 0.28$ for all analyses), even though Ranch Hands in the medium category of initial dioxin had noticeably more abnormalities than Ranch Hands in the low or high categories. The percentages of abnormalities for the low, medium, and high categories of initial dioxin were 1.7, 6.9, and 3.5 respectively. Covariate adjustment in Model 2 accounted for age. By contrast, the unadjusted analysis for Model 3 found a significantly higher percentage of urinary red blood cell count abnormalities in the high Ranch Hand category (5.8%) than in the Comparison category (2.0%) (Table 17-6(e): $p=0.002$, Est. RR=3.00, 95% C.I.=[1.51, 5.93]). The unadjusted relative risk was also significant for the low plus high Ranch Hand category (Table 17-6(e): $p=0.019$, Est. RR=2.10, 95% C.I.=[1.13, 3.90]). In the low plus high category, 4.1 percent of participants had urinary red blood cell count abnormalities.

The adjusted analysis for Model 3 contained a significant categorized dioxin-by-occupation interaction (Table 17-6(f): $p=0.013$) plus two significant covariates, age and race. Appendix Table M-2-3 displays results stratified by occupation. To examine the relationship

Table 17-5.
Analysis of Urinary Protein

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Present**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***950***	***4.6***	***1.02 (0.68,1.53)***	***0.995***
	Comparison	***1,279***	***4.5***		
Officer	Ranch Hand	367	4.6	1.69 (0.82,3.48)	0.207
	Comparison	502	2.8		
Enlisted Flyer	Ranch Hand	161	3.7	0.67 (0.24,1.86)	0.603
	Comparison	202	5.4		
Enlisted Groundcrew	Ranch Hand	422	5.0	0.86 (0.49,1.51)	0.701
	Comparison	575	5.7		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***1.00 (0.66,1.51)***	***0.999***	AGE (p=0.006) OCC (p=0.038) DIAB (p<0.001)
Officer	1.52 (0.73,3.16)	0.263	
Enlisted Flyer	0.70 (0.25,1.96)	0.493	
Enlisted Groundcrew	0.87 (0.49,1.55)	0.634	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 17-5. (Continued)
Analysis of Urinary Protein

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Present	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	173	3.5	1.18 (0.87,1.59)	0.287
Medium	173	3.5		
High	172	5.2		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
518	1.14 (0.85,1.54)	0.383	DIAB (p=0.015)

[a] Adjusted for percent body fat at the time of duty and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 17-5. (Continued)
Analysis of Urinary Protein

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Present	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,062	4.5		
Background RH	374	4.8	1.31 (0.75,2.31)	0.345
Low RH	259	3.5	0.67 (0.32,1.39)	0.280
High RH	259	4.6	0.87 (0.45,1.68)	0.677
Low plus High RH	518	4.1	0.77 (0.45,1.31)	0.334

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,061			AGE (p=0.062) OCC (p=0.078) DIAB (p<0.001)
Background RH	373	1.55 (0.85,2.83)	0.153	
Low RH	259	0.60 (0.28,1.28)	0.188	
High RH	259	0.76 (0.38,1.51)	0.427	
Low plus High RH	518	0.68 (0.39,1.18)	0.168	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 17-5. (Continued)
Analysis of Urinary Protein

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Present/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	4.1 (295)	5.0 (299)	4.0 (298)	1.09 (0.88,1.36)	0.417
5	4.0 (300)	4.1 (296)	5.1 (296)	1.09 (0.90,1.32)	0.361
6[c]	4.0 (299)	4.1 (296)	5.1 (296)	1.07 (0.88,1.31)	0.500

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	891	1.08 (0.85,1.36)**	0.538**	CURR*DIAB (p=0.004) AGE*RACE (p=0.018)
5	891	1.06 (0.86,1.30)**	0.576**	CURR*DIAB (p=0.012) AGE*RACE (p=0.020)
6[d]	890	1.07 (0.86,1.34)**	0.536**	CURR*DIAB (p=0.011) AGE*RACE (p=0.019)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interaction ($p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table M-2-2 for further analysis of this interaction.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.
CURR = Log_2 (current dioxin + 1).

Table 17-6.
Analysis of Urinary Red Blood Cell Count

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	Group	n	Percent Abnormal	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***950***	***3.3***	***1.40 (0.84,2.34)***	***0.237***
	Comparison	***1,279***	***2.3***		
Officer	Ranch Hand	367	2.5	2.08 (0.73,5.89)	0.254
	Comparison	502	1.2		
Enlisted Flyer	Ranch Hand	161	2.5	1.26 (0.31,5.12)	0.999
	Comparison	202	2.0		
Enlisted Groundcrew	Ranch Hand	422	4.3	1.24 (0.65,2.37)	0.636
	Comparison	575	3.5		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks[a]
All	***1.41 (0.84,2.35)***	***0.190***	AGE (p=0.014) RACE (p=0.025) OCC (p=0.005)
Officer	2.04 (0.72,5.80)	0.179	
Enlisted Flyer	1.27 (0.31,5.17)	0.741	
Enlisted Groundcrew	1.24 (0.65,2.38)	0.518	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 17-6. (Continued)
Analysis of Urinary Red Blood Cell Count

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	173	1.7	1.10 (0.79,1.52)	0.582
Medium	173	6.9		
High	172	3.5		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
518	1.21 (0.86,1.69)	0.282	AGE (p=0.055)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 17-6. (Continued)
Analysis of Urinary Red Blood Cell Count

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,062	2.0		
Background RH	374	2.1	1.08 (0.47,2.47)	0.858
Low RH	259	2.3	1.21 (0.48,3.03)	0.688
High RH	259	5.8	3.00 (1.51,5.93)	0.002
Low plus High RH	518	4.1	2.10 (1.13,3.90)	0.019

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,062			DXCAT*OCC (p=0.013) AGE (p=0.016) RACE (p=0.006)
Background RH	374	1.17 (0.50,2.75)**	0.712**	
Low RH	259	1.10 (0.44,2.79)**	0.835**	
High RH	259	2.98 (1.45,6.14)**	0.003**	
Low plus High RH	518	1.97 (1.05,3.68)**	0.035**	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Categorized dioxin-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model after deletion of this interaction; refer to Appendix Table M-2-3 for further analysis of this interaction.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.
DXCAT = Categorized dioxin.

Table 17-6. (Continued)
Analysis of Urinary Red Blood Cell Count

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Abnormal/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	1.7 (295)	3.3 (299)	4.7 (298)	1.18 (0.92,1.50)	0.197
5	1.7 (300)	3.4 (296)	4.7 (296)	1.16 (0.93,1.44)	0.194
6[c]	1.7 (299)	3.4 (296)	4.7 (296)	1.16 (0.92,1.46)	0.224

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	892	1.13 (0.86,1.50)**	0.384**	CURR*OCC (p=0.013)
5	892	1.12 (0.87,1.43)**	0.371**	CURR*OCC (p=0.024)
6[d]	891	1.11 (0.86,1.45)**	0.417**	CURR*OCC (p=0.019)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin +1)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table M-2-3 for further analysis of this interaction.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

between categorized dioxin and urinary red blood cell count, the categorized dioxin-by-occupation interaction was removed from the adjusted analysis of Model 3. Without the interaction, the relative risk for the high Ranch Hand category remained significant after adjusting for age, race, and occupation (Table 17-6(f): p=0.003, Adj. RR=2.98, 95% C.I.=[1.45, 6.14]). In addition, a significant adjusted relative risk was observed for the low plus high Ranch Hand category (Table 17-6(f): p=0.035, Adj. RR=1.97, 95% C.I.=[1.05, 3.68]).

As shown in Table 17-6(g), the unadjusted results for Models 4 through 6 did not display a significant association between urinary red blood cell count and current dioxin (p>0.19 for each model). Each of the adjusted analyses for Models 4, 5, and 6 contained a significant current dioxin-by-occupation interaction (Table 17-6(h): p=0.013, p=0.024, and p=0.019 respectively). Appendix Table M-2-3 displays stratified results for this interaction. The current dioxin-by-occupation interaction was the only covariate in Models 4 through 6. Current dioxin was not found to be significantly associated with urinary protein when current dioxin-by-occupation was removed from the final adjusted models (Table 17-6(g,h): p>0.37 for each model).

Urinary White Blood Cell Count

The unadjusted and adjusted analyses of Model 1 did not find a significant difference in abnormal urinary white blood cell counts between the Ranch Hand and Comparison groups (Table 17-7(a,b): p=0.222 and p=0.208 respectively). The final model in the adjusted analysis for Model 1 contained the covariates age, occupation, and diabetic class. However, stratifying the Model 1 analyses by occupation revealed a statistically significant association between group and urinary white blood cell count for enlisted groundcrew. For the unadjusted analysis, the percentage of enlisted groundcrew Ranch Hands with abnormalities (4.5%) was significantly greater than the percentage of enlisted groundcrew Comparisons with abnormalities (2.1%) (Table 17-7(a): p=0.047, Est. RR=2.21, 95% C.I.=[1.06, 4.61]). The relative risk remained significant after adjusting for age, occupation, and diabetic class (Table 17-7(b): p=0.033, Adj. RR=2.23, 95% C.I.=[1.07, 4.67]).

The initial dioxin and categorized dioxin analyses (Models 2 and 3) for urinary white blood cell count did not uncover any statistically significant results (Table 17-7(c-f): p>0.16 for all analyses). For Model 2, the final model for the adjusted analysis was the same as the unadjusted model, whereas the adjusted analysis for Model 3 included the covariates age, occupation, and race.

Similar to the results of Models 2 and 3, the unadjusted and adjusted analyses for Models 4 through 6 did not detect a significant relationship between urinary white blood cell count and current dioxin (Table 17-7(g,h): p>0.42 for all analyses). For each of the three models, the adjusted results accounted for the covariates age and occupation.

Serum Creatinine

Examination of the unadjusted results for Model 1 revealed no significant group difference in the mean levels of serum creatinine (Table 17-8(a): p>0.77 for all contrasts).

Table 17-7.
Analysis of Urinary White Blood Cell Count

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Abnormal**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	*Ranch Hand*	*950*	*3.5*	*1.40 (0.86,2.30)*	*0.222*
	Comparison	*1,279*	*2.5*		
Officer	Ranch Hand	367	1.9	0.96 (0.36,2.54)	0.999
	Comparison	502	2.0		
Enlisted Flyer	Ranch Hand	161	4.3	0.87 (0.32,2.35)	0.984
	Comparison	202	5.0		
Enlisted Groundcrew	Ranch Hand	422	4.5	2.21 (1.06,4.61)	0.047
	Comparison	575	2.1		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	*1.38 (0.84,2.27)*	*0.208*	AGE (p=0.015) OCC (p=0.007) DIAB (p=0.082)
Officer	0.91 (0.34,2.42)	0.850	
Enlisted Flyer	0.87 (0.32,2.36)	0.792	
Enlisted Groundcrew	2.23 (1.07,4.67)	0.033	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 17-7. (Continued)
Analysis of Urinary White Blood Cell Count

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	173	3.5	0.94 (0.66,1.34)	0.736
Medium	173	4.0		
High	172	3.5		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[a]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
518	0.94 (0.66,1.34)	0.736	

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 17-7. (Continued)
Analysis of Urinary White Blood Cell Count

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	**n**	**Percent Abnormal**	**Est. Relative Risk (95% C.I.)[ab]**	**p-Value**
Comparison	1,062	2.4		
Background RH	374	2.4	1.06 (0.49,2.30)	0.887
Low RH	259	3.5	1.45 (0.67,3.16)	0.346
High RH	259	3.9	1.63 (0.77,3.45)	0.202
Low plus High RH	518	3.7	1.54 (0.84,2.83)	0.165

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	**n**	**Adj. Relative Risk (95% C.I.)[ac]**	**p-Value**	**Covariate Remarks**
Comparison	1,062			AGE (p=0.005) OCC (p=0.046) RACE (p=0.133)
Background RH	374	1.21 (0.55,2.68)	0.640	
Low RH	259	1.37 (0.62,2.99)	0.434	
High RH	259	1.47 (0.68,3.18)	0.333	
Low plus High RH	518	1.42 (0.76,2.62)	0.270	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA, and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 17-7. (Continued)
Analysis of Urinary White Blood Cell Count

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Abnormal/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	2.4 (295)	3.0 (299)	4.0 (298)	1.08 (0.84,1.40)	0.533
5	2.3 (300)	3.0 (296)	4.1 (296)	1.06 (0.85,1.33)	0.579
6[c]	2.3 (299)	3.0 (296)	4.1 (296)	1.10 (0.87,1.40)	0.424

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	892	0.95 (0.72,1.24)	0.684	AGE (p=0.023) OCC (p=0.008)
5	892	0.95 (0.75,1.19)	0.644	AGE (p=0.023) OCC (p=0.007)
6[d]	891	0.98 (0.76,1.26)	0.881	AGE (p=0.018) OCC (p=0.008)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 17-8.
Analysis of Serum Creatinine (mg/dl)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Mean[a]**	**Difference of Means (95% C.I.)[b]**	**p-Value[c]**
All	***Ranch Hand***	***952***	***0.9741***	***0.0005 --***	***0.943***
	Comparison	***1,280***	***0.9737***		
Officer	Ranch Hand	367	0.9792	-0.0002 --	0.981
	Comparison	502	0.9795		
Enlisted Flyer	Ranch Hand	162	0.9616	0.0044 --	0.777
	Comparison	202	0.9572		
Enlisted Groundcrew	Ranch Hand	423	0.9746	0.0002 --	0.988
	Comparison	576	0.9744		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED						
Occupational Category	**Group**	**n**	**Adj. Mean[a]**	**Difference of Adj. Means (95% C.I.)[b]**	**p-Value[c]**	**Covariate Remarks[d]**
All	***Ranch Hand***	***951***	***1.0031*****	***0.0002 --*****	***0.972*****	GROUP*DIAB (p=0.006)
	Comparison	***1,279***	***1.0028*****			RACE (p<0.001)
Officer	Ranch Hand	367	1.0057**	0.0010 --**	0.929**	AGE*DIAB (p=0.041)
	Comparison	502	1.0047**			OCC*DIAB (p=0.015)
Enlisted Flyer	Ranch Hand	162	0.9817**	0.0036 --**	0.831**	
	Comparison	202	0.9782**			
Enlisted Groundcrew	Ranch Hand	422	1.0235**	-0.0017 --**	0.873**	
	Comparison	575	1.0252**			

[a] Transformed from natural logarithm scale.

[b] Difference of adjusted means after transformation to original scale; confidence interval on difference of adjusted means not presented because analysis was performed on natural logarithm scale.

[c] P-value is based on difference of means on natural logarithm scale.

[d] Covariates and associated p-values correspond to final model based on all participants with available data.

** Group-by-covariate interaction ($p \leq 0.05$); adjusted mean, difference of adjusted means, confidence interval, and p-value derived from a model after deletion of this interaction; refer to Appendix Table M-2-4 for further analysis of this interaction.

Table 17-8. (Continued)
Analysis of Serum Creatinine (mg/dl)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	174	1.0058	1.0063	0.005	-0.0093 (0.0066)	0.161
Medium	173	0.9564	0.9568			
High	173	0.9680	0.9670			

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED						
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[d]			
Initial Dioxin	n	Adj. Mean[ad]	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
Low	174	1.0413**	0.061	-0.0086 (0.0069)**	0.214**	INIT*DIAB (p=0.017) RACE (p=0.091) AGE*DIAB (p=0.018)
Medium	173	0.9949**				
High	173	1.0030**				

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Slope and standard error based on natural logarithm of serum creatinine versus $\log_2$ (initial dioxin).

[d] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Log_2 (initial dioxin)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted mean, slope, standard error, and p-value derived from a model after deletion of this interaction; refer to Appendix Table M-2-4 for further analysis of this interaction.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 17-8. (Continued)
Analysis of Serum Creatinine (mg/dl)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED					
Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,063	0.9717	0.9716		
Background RH	374	0.9647	0.9676	-0.0041--	0.678
Low RH	260	0.9910	0.9894	0.0178--	0.116
High RH	260	0.9624	0.9600	-0.0116--	0.298
Low plus High RH	520	0.9766	0.9746	0.0030--	0.728

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED					
Dioxin Category	n	Adj. Mean[ae]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]	Covariate Remarks
Comparison	1,062	0.9953**			DXCAT*DIAB (p=0.002) AGE*RACE (p=0.050) AGE*DIAB (p=0.032) OCC*DIAB (p=0.018)
Background RH	373	0.9872**	-0.0081--**	0.424**	
Low RH	260	1.0095**	0.0142--**	0.217**	
High RH	260	0.9893**	-0.0060--**	0.606**	
Low plus High RH	520	1.0001**	0.0048--**	0.624**	

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA, and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Difference of adjusted means after transformation to original scale; confidence interval on difference of adjusted means not presented because analysis was performed on natural logarithm scale.

[d] P-value is based on difference of means on natural logarithm scale.

[e] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Categorized dioxin-by-covariate interaction ($p \leq 0.05$); adjusted mean, difference of adjusted means, confidence interval, and p-value derived from a model after deletion of this interaction; refer to Appendix Table M-2-4 for further analysis of this interaction.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 17-8. (Continued)
Analysis of Serum Creatinine (mg/dl)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED						
	Current Dioxin Category Mean[a]/(n)			Analysis Results for Log_2 (Current Dioxin + 1)		
Model[b]	Low	Medium	High	R^2	Slope (Std. Error)[c]	p-Value
4	0.9679 (295)	0.9850 (300)	0.9618 (299)	<0.001	0.0011 (0.0042)	0.797
5	0.9635 (300)	0.9840 (297)	0.9674 (297)	<0.001	0.0021 (0.0036)	0.571
6[d]	0.9646 (299)	0.9840 (297)	0.9674 (297)	<0.001	0.0007 (0.0039)	0.863

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED							
	Current Dioxin Category Adjusted Mean[a]/(n)			Analysis Results for Log_2 (Current Dioxin + 1)			
Model[b]	Low	Medium	High	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
4	1.0155 (294)	1.0251 (300)	1.0080 (299)	0.035	0.0017 (0.0044)	0.697	RACE (p=0.001) AGE*DIAB (p=0.001)
5	1.0100 (299)	1.0224 (297)	1.0134 (297)	0.035	0.0027 (0.0037)	0.473	RACE (p=0.001) AGE*DIAB (p=0.001)
6[e]	1.0130 (298)	1.0227 (297)	1.0113 (297)	0.035	0.0010 (0.0040)	0.796	RACE (p=0.001) AGE*DIAB (p=0.001)

[a] Transformed from natural logarithm scale.

[b] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[c] Slope and standard error based on natural logarithm of serum creatinine versus log_2 (current dioxin + 1).

[d] Adjusted for log_2 total lipids.

[e] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

The adjusted analysis of Model 1 found a significant group-by-diabetic class interaction (Table 17-8(b): $p=0.006$). Appendix Table M-2-4 presents results stratified by each level of diabetic class. Race and the age-by-diabetic class and occupation-by-diabetic class interactions were also significant in the final model. Removing the group-by-diabetic class interaction from the adjusted model resulted in no significant association between group and serum creatinine (Table 17-8(b): $p>0.83$ for all contrasts).

The unadjusted analyses for Models 2 and 3 did not show initial dioxin or categorized dioxin to be significantly associated with serum creatinine (Table 17-8(c,e): $p>0.11$ for all analyses). However, the adjusted analysis for Model 2 revealed a significant initial dioxin-by-diabetic class interaction (Table 17-8(d): $p=0.017$). Appendix Table M-2-4 displays results stratified by diabetic class. The race covariate and the age-by-diabetic class interaction also were retained in the adjusted analysis for Model 2. No significant relationship between initial dioxin and serum creatinine was observed when initial dioxin-by-diabetic class was removed from the final adjusted model (Table 17-8(d): $p=0.214$). The categorized dioxin-by-diabetic class adjusted analysis of Model 3 (Table 17-8(f): $p=0.002$). Appendix Table M-2-4 presents results stratified by diabetic class. The interactions age-by-race, age-by-diabetic class, and occupation-by-diabetic class also were significant in the adjusted analysis of Model 3. After deleting the categorized dioxin-by-diabetic class interaction from the final model, serum creatinine was not significantly associated with current dioxin (Table 17-8(f): $p>0.21$ for all contrasts).

No significant association between current dioxin and serum creatinine was detected in the analyses of Models 4 through 6 (Table 17-8(g,h): $p>0.47$ for all analyses). Each of the three models adjusted for a race covariate and the age-by-diabetic class interaction.

Urine Specific Gravity

The Model 1 analysis did not detect a significant group difference in the mean levels of urine specific gravity (Table 17-9(a,b): $p>0.15$ for all analyses). The adjusted analysis accounted for the occupation covariate and the age-by-diabetic class interaction.

The initial and categorized dioxin results (Models 2 and 3) also were not significant (Table 17-9(c-f): $p>0.14$ for unadjusted and adjusted analyses). Model 2 had a significant initial dioxin-by-age interaction in the final adjusted model (Table 17-9(d): $p=0.024$). Appendix Table M-2-5 presents stratified results to examine this interaction. Besides the initial dioxin-by-age interaction, occupation was significant in the adjusted analysis of Model 2. After deleting the initial dioxin-by-age interaction from the final model, urine specific gravity was not significantly associated with initial dioxin (Table 17-9(d): $p=0.231$). For Model 3, covariate adjustment accounted for occupation and diabetic class.

The unadjusted results for Models 4 through 6 showed a significant positive association between current dioxin levels and urine specific gravity (Table 17-9(g): $p=0.013$, Est. slope=0.0004; $p=0.007$, Est. slope=0.0003; $p=0.027$, Est. slope=0.0003 for Models 4, 5, and 6 respectively). The adjusted results were identical to the unadjusted results for Models 4 and 5 because no covariates were retained. By contrast, the association with current dioxin became nonsignificant in Model 6 after adjusting for occupation (Table 17-9(h): $p=0.123$, Adj. slope=0.0002).

Table 17-9.
Analysis of Urine Specific Gravity

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	Group	n	Mean	Difference of Means (95% C.I.)	p-Value
All	***Ranch Hand***	***950***	***1.0187***	***-0.0002 (-0.0007,0.0003)***	***0.489***
	Comparison	***1,279***	***1.0189***		
Officer	Ranch Hand	367	1.0183	0.0002 (-0.0007,0.0010)	0.662
	Comparison	502	1.0181		
Enlisted Flyer	Ranch Hand	161	1.0177	-0.0010 (-0.0025,0.0005)	0.190
	Comparison	202	1.0187		
Enlisted Groundcrew	Ranch Hand	422	1.0195	-0.0002 (-0.0010,0.0006)	0.597
	Comparison	575	1.0197		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED						
Occupational Category	Group	n	Adj. Mean	Difference of Adj. Means (95% C.I.)	p-Value	Covariate Remarks[a]
All	***Ranch Hand***	***949***	***1.0189***	***-0.0002 (-0.0008,0.0003)***	***0.430***	OCC (p<0.001) AGE*DIAB (p=0.048)
	Comparison	***1,278***	***1.0192***			
Officer	Ranch Hand	367	1.0187	0.0001 (-0.0007,0.0010)	0.762	
	Comparison	502	1.0186			
Enlisted Flyer	Ranch Hand	161	1.0181	-0.0010 (-0.0023,0.0004)	0.152	
	Comparison	202	1.0190			
Enlisted Groundcrew	Ranch Hand	421	1.0198	-0.0002 (-0.0010,0.0006)	0.554	
	Comparison	574	1.0200			

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 17-9. (Continued)
Analysis of Urine Specific Gravity

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[a]		
Initial Dioxin	n	Mean	Adj. Mean[a]	R^2	Slope (Std. Error)	p-Value
Low	173	1.0183	1.0184	0.028	0.0003 (0.0002)	0.142
Medium	173	1.0192	1.0192			
High	172	1.0194	1.0193			

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED						
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[b]			
Initial Dioxin	n	Adj. Mean[b]	R^2	Adj. Slope (Std. Error)	p-Value	Covariate Remarks
Low	173	1.0182**	0.048	0.0003 (0.0002)**	0.231**	INIT*AGE (p=0.024) OCC (p=0.033)
Medium	173	1.0190**				
High	172	1.0189**				

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Log_2 (initial dioxin)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted mean, adjusted slope, standard error, and
p-value derived from a model after deletion of this interaction; refer to Appendix Table M-2-5 for further analysis of this interaction.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 17-9. (Continued)
Analysis of Urine Specific Gravity

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED					
Dioxin Category	n	Mean	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)	p-Value
Comparison	1,062	1.0189	1.0189		
Background RH	374	1.0183	1.0186	-0.0003 (-0.0011,0.0004)	0.385
Low RH	259	1.0187	1.0186	-0.0003 (-0.0011,0.0006)	0.528
High RH	259	1.0192	1.0190	0.0001 (-0.0008,0.0009)	0.852
Low plus High RH	518	1.0190	1.0188	-0.0001 (-0.0008,0.0006)	0.774

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED					
Dioxin Category	n	Adj. Mean[b]	Difference of Adj. Mean vs. Comparisons (95% C.I.)	p-Value	Covariate Remarks
Comparison	1,061	1.0191			OCC (p=0.001) DIAB (p=0.132)
Background RH	373	1.0190	-0.0001 (-0.0009,0.0007)	0.820	
Low RH	259	1.0188	-0.0003 (-0.0011,0.0006)	0.549	
High RH	259	1.0188	-0.0003 (-0.0012,0.0006)	0.507	
Low plus High RH	518	1.0188	-0.0003 (-0.0010,0.0004)	0.414	

[a] Adjusted for percent body fat at the time of duty in SEA, and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 17-9. (Continued)
Analysis of Urine Specific Gravity

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED						
	Current Dioxin Category Mean/(n)			Analysis Results for Log_2 (Current Dioxin + 1)		
Model[a]	Low	Medium	High	R^2	Slope (Std. Error)	p-Value
4	1.0183 (295)	1.0185 (299)	1.0192 (298)	0.007	0.0004 (0.0001)	0.013
5	1.0180 (300)	1.0187 (296)	1.0194 (296)	0.008	0.0003 (0.0001)	0.007
6[b]	1.0180 (299)	1.0187 (296)	1.0194 (296)	0.008	0.0003 (0.0001)	0.027

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED							
	Current Dioxin Category Adjusted Mean/(n)			Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	Low	Medium	High	R^2	Adj. Slope (Std. Error)	p-Value	Covariate Remarks
4	1.0183 (295)	1.0185 (299)	1.0192 (298)	0.007	0.0004 (0.0001)	0.013	
5	1.0180 (300)	1.0187 (296)	1.0194 (296)	0.008	0.0003 (0.0001)	0.007	
6[c]	1.0180 (299)	1.0186 (296)	1.0190 (296)	0.013	0.0002 (0.0002)	0.123	OCC (p=0.135)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Adjusted for log_2 total lipids.

[c] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Longitudinal Analysis

Longitudinal analyses were conducted on four variables—urinary protein, urinary red blood cell count, urinary white blood cell count, and urine specific gravity—to examine whether changes across time differed with respect to group membership (Model 1), initial dioxin (Model 2), and categorized dioxin (Model 3). Models 4, 5, and 6 were not examined in longitudinal analyses because current dioxin, the measure of exposure in these models, changes over time and is not available for all participants for 1982, 1985, or 1992. The longitudinal analyses for urinary protein investigated the difference between the 1982 examination and the 1992 examination, because the measurement technique and abnormal cutpoint remained unchanged. Measurement procedures at the 1982 examination differed from the techniques used at subsequent examinations for urinary red blood cell count and urine specific gravity. For the detection of urinary red blood cells, microscopic observation used at the 1985, 1987, and 1992 examinations replaced reagent strip testing used during the 1982 examination; and the multistick procedure incorporated at the 1985, 1987, and 1992 examinations replaced the falling drop method used during the 1982 examination for measuring urine specific gravity. Thus, longitudinal analyses for urinary red blood cell count and urine specific gravity studied changes between the 1985 examination and the 1992 examination. The longitudinal analyses for urinary white blood cell count investigated changes between the 1985 and 1992 examinations because the abnormal cutpoint in 1982 (>4 WBC per HPF) from the Kelsey-Sebold clinic differed from the cutpoint used at the 1985, 1987, and 1992 SCRF examinations (>2 WBC per HPF).

The longitudinal analyses for the discrete variables (urinary protein, urinary red blood cell count, urinary white blood cell count) examined relative risks at the 1992 examination for participants who were classified as normal at the earlier examination. Participants considered abnormal in 1982 (or 1985, as applicable) were excluded because the focus of the analyses was on investigating the temporal effects of dioxin during the period between 1982 or 1985 and 1992. Participants considered abnormal in 1982 or 1985 were already abnormal before this period; consequently, only participants considered normal at the 1982 or 1985 examination were considered to be at risk when the effects of dioxin over time are explored. The rate of abnormalities under this restriction approximates an incidence rate between 1982 or 1985 and 1992. All three models were adjusted for age; Models 2 and 3 were also adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

The longitudinal analysis for the continuous variable, urine specific gravity, examined the paired difference between the measurements from 1985 and 1992. These paired differences measured the change in urine specific gravity over time. Each of the three models used in the longitudinal analysis were adjusted for age and urine specific gravity measured in 1985. The analyses of Models 2 and 3 were also adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

Laboratory Examination Variables

Urinary Protein

The longitudinal analysis for Model 1 did not find a significant group difference in the presence of urinary protein for participants who had an absence of urinary protein in 1982 (Table 17-10(a): $p>0.27$ for all contrasts). Similarly, the analysis of Model 3 did not detect a significant relationship between urinary protein and categorized dioxin (Table 17-10(c): $p>0.14$ for all contrasts).

By contrast, Model 2 detected a marginally significant positive association between urinary protein and initial dioxin (Table 17-10(b): $p=0.065$, Adj. RR=1.38, 95% C.I.=[0.98, 1.94]). Of the Ranch Hand cohort without urinary protein in 1982, 5.4 percent of the participants in the high category of initial dioxin had urinary protein at the 1992 examination, while the percentages of abnormalities in the low and medium categories were 3.0 and 2.4 percent respectively.

Urinary Red Blood Cell Count

Longitudinal analyses for urinary red blood cell count were conditioned on participants without evidence of urinary red blood cells in 1985. No statistically significant results were detected with respect to group differences, associations with initial dioxin, or associations with categorized dioxin (Table 17-11(a-c): $p>0.14$ for all analyses).

In both the Ranch Hand and Comparison cohorts, the percentage of participants with urinary red blood cells in 1982 showed a marked increase between 1982 and 1985 and a decrease between 1985 and 1992. The increase between 1982 and 1985 was most likely due to the change in measurement method. The decrease in 1992 may have resulted in part because the 1985 examination defined presence as at least one urinary red blood cell in contrast to the 1992 examination, which defined an abnormality as more than two urinary red blood cells.

Urinary White Blood Cell Count

The longitudinal analysis of Model 1 did not uncover a significant overall group difference for urinary white blood cell counts (Table 17-12(a): $p=0.204$). However, stratifying the Model 1 analysis by occupation revealed a marginally significant adjusted relative risk for the enlisted groundcrew (Table 17-12(a): $p=0.053$, Adj. RR=2.51, 95% C.I.=[0.99, 6.39]). Of enlisted groundcrew who had no evidence of urinary white blood cells at the 1985 examination, Ranch Hands were more than twice as likely than Comparisons to have urinary white blood cells at the 1992 examination (Table 17-12(a): 3.7% vs. 1.5%).

Displayed in Table 17-12(b), the results of the Model 2 analysis did not reveal a significant association between urinary white blood cell count and initial dioxin ($p=0.770$). The longitudinal analysis for Model 3 detected a significant relative risk for the low plus high Ranch Hand category (Table 17-12(c): $p=0.028$, Adj. RR=2.41, 95% C.I.=[1.10, 5.30]).

Table 17-10.
Longitudinal Analysis of Urinary Protein

a) MODEL 1: RANCH HANDS VS. COMPARISONS					
		Percent Present/(n) Examination			
Occupational Category	Group	1982	1985	1987	1992
All	***Ranch Hand***	***1.3***	***3.1***	***4.4***	***4.5***
		(898)	***(876)***	***(867)***	***(898)***
	Comparison	***1.5***	***2.6***	***3.9***	***4.4***
		(1,062)	***(1,039)***	***(1,036)***	***(1,062)***
Officer	Ranch Hand	1.8	2.1	4.2	4.7
		(340)	(335)	(334)	(340)
	Comparison	0.7	1.0	1.8	3.0
		(403)	(395)	(391)	(403)
Enlisted Flyer	Ranch Hand	1.3	1.3	2.6	3.8
		(158)	(156)	(153)	(158)
	Comparison	1.1	3.5	5.8	5.1
		(175)	(172)	(174)	(175)
Enlisted Groundcrew	Ranch Hand	1.0	4.7	5.3	4.5
		(400)	(385)	(380)	(400)
	Comparison	2.3	3.6	4.9	5.4
		(484)	(472)	(471)	(484)

		Absent in 1982			
Occupational Category	Group	n in 1992	Percent Present in 1992	Adj. Relative Risk (95% C.I.)[a]	p-Value[a]
All	***Ranch Hand***	***886***	***4.0***	***0.99 (0.63,1.57)***	***0.977***
	Comparison	***1,046***	***4.0***		
Officer	Ranch Hand	334	4.2	1.56 (0.70,3.49)	0.279
	Comparison	400	2.8		
Enlisted Flyer	Ranch Hand	156	3.9	0.83 (0.28,2.44)	0.729
	Comparison	173	4.6		
Enlisted Groundcrew	Ranch Hand	396	3.8	0.80 (0.41,1.56)	0.510
	Comparison	473	4.9		

[a] Relative risk, confidence interval, and p-value are in reference to a contrast of 1982 and 1992 results; results adjusted for age in 1992.

Note: Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations. Statistical analyses are based only on participants who had no urinary protein present in 1982 (see Chapter 7, Statistical Methods).

Table 17-10. (Continued)
Longitudinal Analysis of Urinary Protein

b) MODEL 2: RANCH HANDS — INITIAL DIOXIN				
	Percent Present/(n) Examination			
Initial Dioxin	1982	1985	1987	1992
Low	0.6 (166)	4.3 (163)	4.9 (165)	3.6 (166)
Medium	1.2 (169)	3.1 (163)	5.5 (165)	3.0 (169)
High	0.0 (167)	3.0 (165)	3.7 (161)	5.4 (167)

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
	Absent in 1982			
Initial Dioxin	n in 1992	Percent Present in 1992	Adj. Relative Risk (95% C.I.)[b]	p-Value
Low	165	3.0	1.38 (0.98,1.94)	0.065
Medium	167	2.4		
High	167	5.4		

[a] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and age in 1992.

[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations. Statistical analyses are based only on participants who had no urinary protein present in 1982 (see Chapter 7, Statistical Methods).

Table 17-10. (Continued)
Longitudinal Analysis of Urinary Protein

c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY				
	Percent Present/(n) Examination			
Dioxin Category	1982	1985	1987	1992
Comparison	1.4 (916)	2.2 (905)	4.1 (906)	4.6 (916)
Background RH	2.4 (341)	2.7 (338)	3.6 (335)	4.7 (341)
Low RH	0.8 (249)	3.3 (243)	5.3 (247)	3.6 (249)
High RH	0.4 (253)	3.6 (248)	4.1 (244)	4.4 (253)
Low plus High RH	0.6 (502)	3.5 (491)	4.7 (491)	4.0 (502)

	Absent in 1982			
Dioxin Category	n in 1992	Percent Present in 1992	Adj. Relative Risk (95% C.I.)[ab]	p-Value[b]
Comparison	903	4.2		
Background RH	333	4.2	1.16 (0.61,2.20)	0.650
Low RH	247	2.8	0.54 (0.23,1.23)	0.143
High RH	252	4.4	0.99 (0.49,2.03)	0.989
Low plus High RH	499	3.6	0.74 (0.41,1.34)	0.324

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and age in 1992.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations. Statistical analyses are based only on participants who had no urinary protein present in 1982 (see Chapter 7, Statistical Methods).

Table 17-11.
Longitudinal Analysis of Urinary Red Blood Cell Count

a) MODEL 1: RANCH HANDS VS. COMPARISONS					
		Percent Abnormal/(n) Examination			
Occupational Category	Group	1982	1985	1987	1992
All	***Ranch Hand***	***1.4 (877)***	***17.8 (912)***	***8.6 (887)***	***3.1 (912)***
	Comparison	***0.8 (1,038)***	***16.2 (1,152)***	***6.8 (1,129)***	***2.3 (1,152)***
Officer	Ranch Hand	1.8 (335)	14.8 (352)	6.4 (345)	2.6 (352)
	Comparison	0.5 (394)	13.1 (444)	5.5 (435)	0.9 (444)
Enlisted Flyer	Ranch Hand	0.6 (156)	17.7 (158)	11.7 (154)	2.5 (158)
	Comparison	1.2 (172)	20.1 (189)	8.1 (186)	2.1 (189)
Enlisted Groundcrew	Ranch Hand	1.3 (386)	20.4 (402)	9.3 (388)	3.7 (402)
	Comparison	0.9 (472)	17.5 (519)	7.5 (508)	3.5 (519)

		Normal in 1985			
Occupational Category	Group	n in 1992	Percent Abnormal in 1992	Adj. Relative Risk (95% C.I.)[a]	p-Value[a]
All	***Ranch Hand***	***750***	***1.6***	***0.91 (0.43,1.91)***	***0.796***
	Comparison	***965***	***1.8***		
Officer	Ranch Hand	300	1.3	1.71 (0.38,7.72)	0.483
	Comparison	386	0.8		
Enlisted Flyer	Ranch Hand	130	2.3	1.16 (0.23,5.90)	0.857
	Comparison	151	2.0		
Enlisted Groundcrew	Ranch Hand	320	1.6	0.61 (0.21,1.78)	0.367
	Comparison	428	2.6		

[a] Relative risk, confidence interval, and p-value are in reference to a contrast of 1985 and 1992 results; results adjusted for age in 1992.

Note: Summary statistics for 1982 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1985, 1987, and 1992 examinations. Statistical analyses are based only on participants who had normal urinary red blood cell counts in 1985 (see Chapter 7, Statistical Methods).

Table 17-11. (Continued)
Longitudinal Analysis of Urinary Red Blood Cell Count

b) MODEL 2: RANCH HANDS — INITIAL DIOXIN				
	Percent Abnormal/(n) Examination			
Initial Dioxin	1982	1985	1987	1992
Low	0.6 (163)	12.6 (167)	7.2 (167)	1.8 (167)
Medium	4.3 (163)	19.2 (167)	12.2 (164)	7.2 (167)
High	0.6 (165)	20.1 (169)	9.2 (163)	3.0 (169)

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
	Normal in 1985			
Initial Dioxin	n in 1992	Percent Abnormal in 1992	Adj. Relative Risk (95% C.I.)[b]	p-Value
Low	146	0.7	1.26 (0.77,2.08)	0.372
Medium	135	4.4		
High	135	1.5		

[a] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and age in 1992.

[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Summary statistics for 1982 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1985, 1987, and 1992 examinations. Statistical analyses are based only on participants who had normal urinary red blood cell counts in 1985 (see Chapter 7, Statistical Methods).

Table 17-11. (Continued)
Longitudinal Analysis of Urinary Red Blood Cell Count

c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY				
	Percent Abnormal/(n) Examination			
Dioxin Category	1982	1985	1987	1992
Comparison	0.9 (904)	16.3 (997)	7.0 (987)	2.0 (997)
Background RH	0.9 (339)	16.9 (361)	7.4 (353)	2.2 (361)
Low RH	2.1 (243)	13.6 (250)	7.7 (248)	2.4 (250)
High RH	1.6 (248)	21.0 (253)	11.4 (246)	5.5 (253)
Low plus High RH	1.8 (491)	17.3 (503)	9.5 (494)	4.0 (503)

	Normal in 1985			
Dioxin Category	n in 1992	Percent Abnormal in 1992	Adj. Relative Risk (95% C.I.)[ab]	p-Value[b]
Comparison	835	1.3		
Background RH	300	1.0	0.78 (0.21,2.83)	0.703
Low RH	216	1.4	0.91 (0.24,3.40)	0.883
High RH	200	3.0	2.17 (0.76,6.19)	0.146
Low plus High RH	416	2.2	1.48 (0.60,3.70)	0.397

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and age in 1992.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Summary statistics for 1982 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1985, 1987, and 1992 examinations. Statistical analyses are based only on participants who had normal urinary red blood cell counts in 1985 (see Chapter 7, Statistical Methods).

Table 17-12.
Longitudinal Analysis of Urinary White Blood Cell Count

a) MODEL 1: RANCH HANDS VS. COMPARISONS

Occupational Category	Group	Percent Abnormal/(n) Examination 1982	1985	1987	1992
All	*Ranch Hand*	*1.5* (*877*)	*10.0* (*912*)	*7.1* (*886*)	*3.5* (*912*)
	Comparison	*2.3* (*1,039*)	*7.8* (*1,153*)	*6.6* (*1,130*)	*2.7* (*1,153*)
Officer	Ranch Hand	1.5 (335)	7.4 (352)	6.1 (345)	2.0 (352)
	Comparison	1.5 (395)	5.8 (445)	7.1 (436)	2.3 (445)
Enlisted Flyer	Ranch Hand	0.6 (156)	10.8 (158)	7.1 (154)	4.4 (158)
	Comparison	2.3 (172)	7.4 (189)	3.8 (186)	5.3 (189)
Enlisted Groundcrew	Ranch Hand	1.8 (386)	11.9 (402)	8.0 (387)	4.5 (402)
	Comparison	3.0 (472)	9.6 (519)	7.3 (508)	2.1 (519)

Occupational Category	Group	Normal in 1985: n in 1992	Normal in 1985: Percent Abnormal in 1992	Adj. Relative Risk (95% C.I.)[a]	p-Value[a]
All	*Ranch Hand*	*821*	*2.4*	*1.53 (0.79,2.93)*	*0.204*
	Comparison	*1,063*	*1.6*		
Officer	Ranch Hand	326	0.9	0.76 (0.18,3.23)	0.715
	Comparison	419	1.2		
Enlisted Flyer	Ranch Hand	141	2.8	0.98 (0.26,3.71)	0.976
	Comparison	175	2.9		
Enlisted Groundcrew	Ranch Hand	354	3.7	2.51 (0.99,6.39)	0.053
	Comparison	469	1.5		

[a] Relative risk, confidence interval, and p-value are in reference to a contrast of 1985 and 1992 results; results adjusted for age in 1992.

Note: Summary statistics for 1982 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1985, 1987, and 1992 examinations. Statistical analyses are based only on participants who had normal urinary white blood cell counts in 1985 (see Chapter 7, Statistical Methods).

Table 17-12. (Continued)
Longitudinal Analysis of Urinary White Blood Cell Count

b) MODEL 2: RANCH HANDS — INITIAL DIOXIN

Initial Dioxin	Percent Abnormal/(n) Examination 1982	1985	1987	1992
Low	3.1 (163)	11.4 (167)	9.6 (166)	3.6 (167)
Medium	2.5 (163)	11.4 (167)	7.3 (164)	4.2 (167)
High	0.6 (165)	10.7 (169)	8.6 (163)	3.6 (169)

Initial Dioxin	Initial Dioxin Category Summary Statistics: Normal in 1985 — n in 1992	Percent Abnormal in 1992	Analysis Results for Log₂ (Initial Dioxin)[a]: Adj. Relative Risk (95% C.I.)[b]	p-Value
Low	148	3.4	0.94 (0.61,1.44)	0.770
Medium	148	3.4		
High	151	2.7		

[a] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and age in 1992.

[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Summary statistics for 1982 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1985, 1987, and 1992 examinations. Statistical analyses are based only on participants who had normal urinary white blood cell counts in 1985 (see Chapter 7, Statistical Methods).

Table 17-12. (Continued)
Longitudinal Analysis of Urinary White Blood Cell Count

c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY				
	Percent Abnormal/(n) Examination			
Dioxin Category	1982	1985	1987	1992
Comparison	2.4 (905)	7.6 (998)	6.6 (988)	2.4 (998)
Background RH	0.9 (339)	8.3 (361)	6.0 (353)	2.5 (361)
Low RH	2.5 (243)	11.6 (250)	8.5 (247)	3.6 (250)
High RH	1.6 (248)	10.7 (253)	8.5 (246)	4.0 (253)
Low plus High RH	2.0 (491)	11.1 (503)	8.5 (493)	3.8 (503)

	Normal in 1985			
Dioxin Category	n in 1992	Percent Abnormal in 1992	Adj. Relative Risk (95% C.I.)[ab]	p-Value[b]
Comparison	922	1.3		
Background RH	331	0.9	0.69 (0.19,2.50)	0.577
Low RH	221	3.2	2.38 (0.92,6.15)	0.074
High RH	226	3.1	2.45 (0.94,6.42)	0.068
Low plus High RH	447	3.1	2.41 (1.10,5.30)	0.028

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and age in 1992.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Summary statistics for 1982 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1985, 1987, and 1992 examinations. Statistical analyses are based only on participants who had normal urinary white blood cell counts in 1985 (see Chapter 7, Statistical Methods).

Only 1.3 percent of Comparisons with normal counts of urinary white blood cells during the 1985 examination had abnormal counts of urinary white blood cells at the 1992 examination, while 3.1 percent of Ranch Hands in the low plus high category of dioxin with normal urinary white blood cells counts in 1985 displayed abnormal urinary white blood cell counts in 1992. In addition, the low Ranch Hand category of dioxin and the high Ranch Hand category of dioxin displayed marginally significant relative risks (Table 17-12(c): p=0.074, Adj. RR=2.38, 95% C.I.=[0.92, 6.15]; p=0.068, Adj. RR=2.45, 95% C.I.=[0.94, 6.42] respectively). Examination of Ranch Hands in the low dioxin category and the high dioxin category with normal urinary white blood cell counts in 1985 revealed that the prevalence rates for abnormal urinary white blood cell counts in 1992 were similar for the two categories (3.2% and 3.1% respectively).

Similar to the urinary red blood cell count findings, the prevalence rate of urinary white blood cells increased substantially between 1982 and 1985, and decreased between 1985 and 1992 in both the Ranch Hand and Comparison groups. The difference between the 1982 and 1985 results is partly because an abnormality in 1982 was defined as >4 WBC per HPF, while in 1985 an abnormality was defined as >2 WBC per HPF.

Urine Specific Gravity

Examination of the paired difference between 1985 and 1992 for urine specific gravity did not uncover a significant group difference (Model 1 analysis, Table 17-13(a): p>0.21 for all contrasts). Also, the analyses of Models 2 and 3 did not find a significant association with initial dioxin or categorized dioxin (Table 17-13(b,c): p>0.17 for all analyses).

DISCUSSION

In clinical practice, the presence of renal or urinary tract disease can be determined with confidence based on the medical history, physical examination, and the five laboratory indices included in the current analysis.

Although subject to some day-to-day variation related to diet and state of hydration, the serum creatinine is considered a reliable index of glomerular filtration, while the integrity and concentrating ability of the renal tubular system are reflected in the urine specific gravity. In documenting the presence of red or white blood cells in significant numbers, the examination of the urinary sediment can provide valuable clues to the presence of a broad range of infectious, inflammatory, and neoplastic conditions intrinsic to the upper and lower urinary tracts.

Pertinent to the interpretation of the renal assessment data and to the covariate associations noted below is the frequent finding in ambulatory medicine of isolated abnormalities in the routine urinalysis of healthy individuals who in fact have no disease of the genitourinary system. With normal fluid balance, the healthy kidneys can excrete up to 100 mg to 150 mg of total protein in 24 hours. The qualitative dipstick test used in the current study is sensitive to protein concentrations as low as 10 mg to 15 mg per deciliter and, particularly in specimens collected after overnight fasting, will often give a trace to 1+ positive reaction in the absence of intrinsic renal disease.

Table 17-13.
Longitudinal Analysis of Urine Specific Gravity

Occupational Category	Group	Mean/(n) Examination 1982	1985	1987	1992	Exam. Mean Change[a]	Difference of Exam. Mean Change	p-Value[b]
a) MODEL 1: RANCH HANDS VS. COMPARISONS								
All	***Ranch Hand***	1.0190 (877)	1.0157 (912)	1.0199 (887)	1.0188 (912)	0.0030	-0.0006	0.268
	Comparison	1.0181 (1,038)	1.0153 (1,152)	1.0200 (1,129)	1.0190 (1,152)	0.0037		
Officer	***Ranch Hand***	1.0211 (335)	1.0148 (352)	1.0191 (345)	1.0184 (352)	0.0035	-0.0001	0.819
	Comparison	1.0156 (394)	1.0146 (444)	1.0189 (435)	1.0182 (444)	0.0036		
Enlisted Flyer	***Ranch Hand***	1.0132 (156)	1.0151 (158)	1.0190 (154)	1.0177 (158)	0.0027	-0.0002	0.349
	Comparison	1.0210 (172)	1.0157 (189)	1.0202 (186)	1.0185 (189)	0.0028		
Enlisted Groundcrew	***Ranch Hand***	1.0195 (386)	1.0167 (402)	1.0209 (388)	1.0195 (402)	0.0028	-0.0013	0.216
	Comparison	1.0191 (472)	1.0157 (519)	1.0209 (508)	1.0198 (519)	0.0040		

[a] Difference between 1992 and 1985 examination means.

[b] Results adjusted for urine specific gravity in 1985 and age in 1992.

Note: Summary statistics for 1982 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1985, 1987, and 1992 examinations.

Table 17-13. (Continued)
Longitudinal Analysis of Urine Specific Gravity

b) MODEL 2: RANCH HANDS — INITIAL DIOXIN						
	Initial Dioxin Category Summary Statistics Mean/(n) Examination				Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	1982	1985	1987	1992	Adj. Slope (Std. Error)	p-Value
Low	1.0148 (163)	1.0149 (167)	1.0199 (167)	1.0183 (167)	0.0003 (0.0002)	0.178
Medium	1.0146 (163)	1.0167 (167)	1.0203 (164)	1.0193 (167)		
High	1.0218 (165)	1.0167 (169)	1.0206 (163)	1.0196 (169)		

[a] Results based on difference between 1992 and 1985 urine specific gravity versus $\log_2$ (initial dioxin); results adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, 1985 urine specific gravity, and age in 1992.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Summary statistics for 1982 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1985, 1987, and 1992 examinations.

Table 17-13. (Continued)
Longitudinal Analysis of Urine Specific Gravity

c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY							
	Mean/(n) Examination						
Dioxin Category	1982	1985	1987	1992	Exam. Mean Change[a]	Difference of Exam. Mean Change[b]	p-Value[c]
Comparison	1.0175 (904)	1.0152 (997)	1.0200 (987)	1.0190 (997)	0.0038		
Background RH	1.0214 (339)	1.0152 (361)	1.0194 (353)	1.0183 (361)	0.0032	-0.0006	0.351
Low RH	1.0124 (243)	1.0153 (250)	1.0200 (248)	1.0187 (250)	0.0035	-0.0003	0.527
High RH	1.0217 (248)	1.0169 (253)	1.0205 (246)	1.0193 (253)	0.0024	-0.0014	0.479
Low plus High RH	1.0171 (491)	1.0161 (503)	1.0203 (494)	1.0190 (503)	0.0029	-0.0008	0.386

[a] Difference between 1992 and 1985 examination means.

[b] Difference between Ranch Hand dioxin category and Comparison category.

[c] Results adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, 1985 urine specific gravity, and age in 1992.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Summary statistics for 1982 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1985, 1987, and 1992 examinations.

Similarly, on microscopic examination of the urinary sediment, it is not unusual to find a few red or white blood cells in the absence of definable neoplastic or inflammatory cause, trauma, or renal calculi. When documented as an isolated finding in the absence of symptoms or other signs, such intermittent microcyturia usually can be considered benign and safely followed over time.

In the current assessment, no significant group differences were noted in the history of urinary tract disease. Furthermore, in the Ranch Hand cohort, there was no evidence linking prior dioxin exposure or the current body burden of dioxin to the occurrence of renal disease or the presence of renal calculi detected by plain films of the abdomen.

In the analyses of laboratory data, several statistically significant associations were documented. Although the prevalence of microhematuria was similar in both groups, Ranch Hands with the highest levels of extrapolated initial dioxin had a significantly higher prevalence of microhematuria than Comparisons in both the unadjusted (5.8% vs. 2.0%, p=0.002) and adjusted (p=0.003) analyses. These results are similar to those documented in the Serum Dioxin Analysis Report, when hematuria was noted in 10.2 percent of Ranch Hands with high initial dioxin levels versus 4.9 percent of those with low exposure. Although not statistically significant, the analyses employing current serum dioxin yielded results consistent with a dose-response effect. Clinically, the finding of hematuria can signal the presence of "silent" renal calculi or neoplastic disease.

The presence of white blood cells in the urine (pyuria) can be a marker for the presence of a urinary tract infection. Though the overall history of renal disease was similar in both cohorts, those Ranch Hands most highly exposed to dioxin, the enlisted groundcrew, had twice the prevalence of pyuria as Comparisons (4.5% vs. 2.1%; p=0.047).

The analysis of urine specific gravity documented a highly significant positive association with current serum dioxin in all models, but the differences in the means are not clinically significant. Analyses of serum creatinine and proteinuria revealed no differences between the cohorts.

Dependent variable-covariate analyses revealed several associations that are well established in clinical practice. The increased occurrence of urinary tract disease in older participants would be expected with benign enlargement of the prostate, as would the more common occurrence of renal calculi. The gradual reduction in renal mass and renal plasma flow that occurs with benign nephrosclerosis is associated with age-related increases in serum creatinine and proteinuria. Blacks, at increased risk for hypertension associated with nephropathy, were found to be at increased risk for proteinuria, hematuria and elevation in the serum creatinine. Finally, in diabetics, the increased occurrence of hypertensive arteriosclerotic vascular disease and urinary tract infections related to glycosuria provide a reasonable explanation for the significant covariate associations with proteinuria, pyuria, and the history of renal disease.

With respect to the variables analyzed longitudinally, there was no evidence of any detriment related to the current body burden of dioxin. Consistent with the exposure analysis results noted above, enlisted groundcrew Ranch Hands were, by longitudinal analysis, twice

as likely as enlisted groundcrew Comparisons to develop pyuria over time. Though this finding raises the possibility of a subtle inflammatory reaction, the similar prevalence of pyuria in Ranch Hands with low (3.3%) and high (3.6%) levels of serum dioxin provides evidence against a dose-response effect.

In summary, the data analyzed in the current section revealed abnormalities in five laboratory indices common in ambulatory practice. With the possible exception of hematuria noted above, there was no consistent evidence for any detriment related to current body burden of dioxin or to the estimated severity of prior exposure.

SUMMARY

Seven dependent variables were analyzed in the Renal Assessment—kidney disease, kidney stones, urinary protein, urinary red blood cell count, urinary white blood cell count, serum creatinine, and urine specific gravity. Subjects' prior history of kidney disease was verified from medical records and the presence of kidney stones by x ray was evaluated during the physical exam. The remaining five variables were measured through laboratory analysis. These seven health endpoints were analyzed for associations with group (Model 1), initial dioxin (Model 2), categorized initial dioxin (Model 3), current lipid-adjusted dioxin (Model 4), and current whole-weight dioxin (Models 5 and 6). Of the seven variables, serum creatinine and urine specific gravity were analyzed in continuous form, while the other five variables were examined in discrete form. In addition, four of the seven variables were examined longitudinally (urinary protein, urinary red blood cell count, urinary white blood cell count, and urine specific gravity). The results of the group, initial dioxin, categorized dioxin and current dioxin analyses are summarized in Tables 17-14 through 17-17. A summary of group-by-covariate and dioxin-by-covariate interactions is found in Table 17-18.

Model 1: Group Analysis

Examination of the unadjusted and adjusted results from Model 1 showed no significant overall group differences among the seven variables. However, when the analyses were stratified by occupation, a significant group difference was detected for urinary white blood cell count in the enlisted groundcrew stratum (Adj. RR=2.23, 95% C.I.=[1.07, 4.67]).

The longitudinal analysis results paralleled these findings. A significant overall group difference was not detected for each of the longitudinal variables. However, stratifying the results by occupation revealed a significant group difference within the enlisted groundcrew stratum for increases in urinary white blood cell count over time (Table 17-12(a): Adj. RR=2.69, 95% C.I.=[1.14, 6.32]). The adjusted relative risks estimated from the Model 1 analysis were based on participants without evidence of urinary white blood cells in 1982.

Model 2: Initial Dioxin Analysis

Reviewing the results of Model 2, kidney stones was the only variable that displayed a significant association with initial dioxin. The unadjusted analysis exhibited a significant decrease in kidney stones with increasing initial dioxin. This association became marginally significant after adjusting for age.

Table 17-14.
Summary of Group Analyses (Model 1) for Renal Variables
(Ranch Hands vs. Comparisons)

Variable	UNADJUSTED			
	All	Officer	Enlisted Flyer	Enlisted Groundcrew
Medical Records				
History of Kidney Disease (D)	NS	NS	NS	ns
Physical Examination				
Kidney Stones (D)	NS	ns	NS	NS
Laboratory				
Urinary Protein (D)	NS	NS	ns	ns
Urinary Red Blood Cell Count (D)	NS	NS	NS	NS
Urinary White Blood Cell Count (D)	NS	ns	ns	+0.047
Serum Creatinine (C)	NS	ns	NS	NS
Urine Specific Gravity (C)	ns	NS	ns	ns

C: Continuous analysis.
D: Discrete analysis.
+: Relative risk $\geq$ 1.00.
NS or ns: Not significant ($p>0.10$).
Note: P-value given if $p\leq0.05$.
A capital "NS" denotes a relative risk of 1.00 or greater for discrete analyses or difference of means nonnegative for continuous analyses. A lower case "ns" denotes relative risk less than 1.00 for discrete analyses or difference of means negative for continuous analyses.

Table 17-14. (Continued)
Summary of Group Analyses (Model 1) for Renal Variables
(Ranch Hands vs. Comparisons)

	ADJUSTED			
Variable	All	Officer	Enlisted Flyer	Enlisted Groundcrew
Medical Records				
History of Kidney Disease (D)	NS	NS	NS	ns
Physical Examination				
Kidney Stones (D)	NS	ns	NS	NS
Laboratory				
Urinary Protein (D)	NS	NS	ns	ns
Urinary Red Blood Cell Count (D)	NS	NS	NS	NS
Urinary White Blood Cell Count (D)	NS	ns	ns	+0.033
Serum Creatinine (C)	**(NS)	**(NS)	**(NS)	**(ns)
Urine Specific Gravity (C)	ns	NS	ns	ns

C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥ 1.00.
NS or ns: Not significant (p>0.10).
**(NS) or **(ns): Group-by-covariate interaction (p≤0.05); not significant when interaction is deleted; refer to Appendix M-2 for further analysis of this interaction.
Note: P-value given if p≤0.05.
A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or difference of means nonnegative for continuous analysis; a lower case "ns" denotes relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

Table 17-15.
Summary of Initial Dioxin Analyses (Model 2) for Renal Variables (Ranch Hands Only)

Variable	Unadjusted	Adjusted
Medical Records		
History of Kidney Disease (D)	ns	ns
Physical Examination		
Kidney Stones (D)	-0.016	**(ns*)
Laboratory		
Urinary Protein (D)	NS	NS
Urinary Red Blood Cell Count (D)	NS	NS
Urinary White Blood Cell Count (D)	ns	ns
Serum Creatinine (C)	ns	**(ns)
Urine Specific Gravity (C)	NS	**(NS)

C: Continuous analysis.
D: Discrete analysis.
-: Relative risk < 1.00.
NS or ns: Not significant ($p > 0.10$).
ns*: Marginally significant ($0.05 < p \leq 0.10$).
**(NS) or **(ns): Log_2 (initial dioxin)-by-covariate interaction ($p \leq 0.05$); not significant when interaction is deleted; refer to Appendix M-2 for further analysis of this interaction.
**(ns*): Log_2 (initial dioxin)-by-covariate interaction ($p \leq 0.05$); marginally significant when interaction is deleted; refer to Appendix M-2 for further analysis of this interaction.
Note: P-value given if $p \leq 0.05$.
A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or nonnegative slope for continuous analysis; a lowercase "ns" denotes relative risk less than 1.00 for discrete analysis or negative slope for continuous analysis.

Table 17-16.
Summary of Categorized Dioxin Analyses (Model 3) for Renal Variables (Ranch Hands vs. Comparisons)

	UNADJUSTED			
Variable	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Medical Records				
History of Kidney Disease (D)	NS	NS	NS	NS
Physical Examination				
Kidney Stones (D)	NS	NS	NS	NS
Laboratory				
Urinary Protein (D)	NS	ns	ns	ns
Urinary Red Blood Cell Count (D)	NS	NS	+0.002	+0.019
Urinary White Blood Cell Count (D)	NS	NS	NS	NS
Serum Creatinine (C)	ns	NS	ns	NS
Urine Specific Gravity (C)	ns	ns	NS	ns

C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥ 1.00.
NS or ns: Not significant (p>0.10).
Note: P-value given if p≤0.05.
A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or difference of means nonnegative for continuous analysis; a lower case "ns" denotes relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

Table 17-16. (Continued)
Summary of Categorized Dioxin Analyses (Model 3) for Renal Variables (Ranch Hands vs. Comparisons)

Variable	ADJUSTED			
	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Medical Records				
History of Kidney Disease (D)	NS	NS	NS	NS
Physical Examination				
Kidney Stones (D)	ns	NS	NS	NS
Laboratory				
Urinary Protein (D)	NS	ns	ns	ns
Urinary Red Blood Cell Count (D)	**(NS)	**(NS)	**(+0.003)	**(+0.035)
Urinary White Blood Cell Count (D)	NS	NS	NS	NS
Serum Creatinine (C)	**(ns)	**(NS)	**(ns)	**(NS)
Urine Specific Gravity (C)	ns	ns	ns	ns

C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥ 1.00.
NS or ns: Not significant ($p>0.10$).
**(NS) or **(ns): Categorized dioxin-by-covariate interaction ($p\leq 0.05$); not significant when interaction is deleted; refer to Appendix M-2 for further analysis of this interaction.
**(...): Categorized dioxin-by-covariate interaction ($p\leq 0.05$); significant when interaction is deleted and p-value is given in parentheses; refer to Appendix M-2 for further analysis of this interaction.
Note: P-value given if $p\leq 0.05$.
A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or difference of means nonnegative for continuous analysis; a lower case "ns" denotes relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

Table 17-17.
Summary of Current Dioxin Analyses (Models 4, 5, and 6) for Renal Variables (Ranch Hands Only)

Variable	UNADJUSTED		
	Model 4: Lipid-Adjusted Current Dioxin	Model 5: Whole-Weight Current Dioxin	Model 6: Whole-Weight Current Dioxin Adjusted for Total Lipids
Medical Records			
History of Kidney Disease (D)	NS	NS	NS
Physical Examination			
Kidney Stones (D)	ns	ns	ns
Laboratory			
Urinary Protein (D)	NS	NS	NS
Urinary Red Blood Cell Count (D)	NS	NS	NS
Urinary White Blood Cell Count (D)	NS	NS	NS
Serum Creatinine (C)	NS	NS	NS
Urine Specific Gravity (C)	+0.013	+0.007	+0.027

C: Continuous analysis.
D: Discrete analysis.
+: Slope nonnegative.
NS or ns: Not significant.
Note: P-value given if $p \leq 0.05$.
A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or nonnegative slope for continuous analysis; a lower case "ns" denotes relative risk less than 1.00 for discrete analysis or negative slope for continuous analysis.

Table 17-17. (Continued)
Summary of Current Dioxin Analyses (Models 4, 5, and 6) for Renal Variables (Ranch Hands Only)

Variable	ADJUSTED		
	Model 4: Lipid-Adjusted Current Dioxin	Model 5: Whole-Weight Current Dioxin	Model 6: Whole-Weight Current Dioxin Adjusted for Total Lipids
Medical Records			
History of Kidney Disease (D)	NS	NS	NS
Physical Examination			
Kidney Stones (D)	ns	ns	ns
Laboratory			
Urinary Protein (D)	**(NS)	**(NS)	**(NS)
Urinary Red Blood Cell Count (D)	**(NS)	**(NS)	**(NS)
Urinary White Blood Cell Count (D)	ns	ns	ns
Serum Creatinine (C)	NS	NS	NS
Urine Specific Gravity (C)	+0.013	+0.007	NS

C: Continuous analysis.
D: Discrete analysis.
+: Slope nonnegative.
NS or ns: Not significant.
**(NS): Log_2 (current dioxin + 1)-by-covariate interaction ($p \leq 0.05$); not significant when interaction is deleted; refer to Appendix M-2 for further analysis of this interaction.
Note: P-value given if $p \leq 0.05$.
A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or nonnegative slope for continuous analysis; a lower case "ns" denotes relative risk less than 1.00 for discrete analysis or negative slope for continuous analysis.

Table 17-18.
Summary of Group-by-Covariate and Dioxin-by-Covariate Interactions from Analyses of Renal Variables

Model	Variable	Covariate
1[a]	Serum Creatinine	Diabetic Class
2[b]	Kidney Stones	Diabetic Class
	Serum Creatinine	Diabetic Class
	Urine Specific Gravity	Age
3[c]	Urinary Red Blood Cell Count	Occupation
	Serum Creatinine	Diabetic Class
4[d]	Urinary Protein	Diabetic Class
	Urinary Red Blood Cell Count	Occupation
5[e]	Urinary Protein	Diabetic Class
	Urinary Red Blood Cell Count	Occupation
6[f]	Urinary Protein	Diabetic Class
	Urinary Red Blood Cell Count	Occupation

[a] Group Analysis (Ranch Hands vs. Comparisons).
[b] Ranch Hand—Log_2 (Initial Dioxin).
[c] Categorized Dioxin.
[d] Ranch Hand—Log_2 (Current Lipid-Adjusted Dioxin + 1).
[e] Ranch Hand—Log_2 (Current Whole-Weight Dioxin + 1).
[f] Ranch Hand—Log_2 (Current Whole-Weight Dioxin + 1) Adjusted for Total Lipids.

The longitudinal analyses of urinary protein revealed a marginally significant positive association with initial dioxin; results for the other variables analyzed longitudinally were not significant.

Model 3: Categorized Dioxin Analysis

For Model 3, urinary red blood cell count was the only variable to display a significant association with categorized dioxin. A significant difference was observed between the high Ranch Hand and Comparison categories in both the unadjusted and adjusted analyses (Adj. RR=2.98, 95% C.I.=[1.45, 6.14]). Also, both analyses detected a significant relative risk for the low plus high Ranch Hand category (Adj. RR=1.97, 95% C.I.=[1.05, 3.68]). The Model 3 longitudinal analyses were not significant.

Models 4, 5, and 6: Current Dioxin Analysis

Urine specific gravity was the only variable in the analyses of Models 4 through 6 to display a significant association with current dioxin. The unadjusted analyses of Models 4 through 6 revealed a significant positive association with current dioxin. The adjusted analyses for Models 4 and 5 were identical to the unadjusted analyses because no covariates were retained in the final models. By contrast, the adjusted Model 6 analysis kept occupation in the final model causing the relationship between urine specific gravity and current dioxin to become nonsignificant.

CONCLUSION

The analysis of the seven renal health endpoints revealed isolated statistically significant findings, but did not reveal consistent evidence for any detriment related to group membership, estimated initial dioxin exposure, or current serum dioxin levels. One finding that deserves scrutiny in future examination cycles is the higher prevalence of urinary red blood cells (microhematuria) for Ranch Hands in the high initial dioxin category relative to the Comparison group. This is consistent with the significant positive dose-response relationship between microhematuria and initial dioxin levels (Ranch Hands only) noted in the results of the 1987 examination. However, none of the other 1992 exposure analysis results were statistically significant for urinary red blood cell count, and the longitudinal analyses indicate that the prevalence of microhematuria has decreased in the Ranch Hand cohort at each of the last two cycles. Clinically, the detection of urinary red blood cells may signal the presence of silent renal calculi or neoplastic disease. The analyses of kidney stones did not support the presence of silent renal calculi. Neoplastic disease is discussed in Chapter 10, Neoplasia.

CHAPTER 17
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CHAPTER 18

ENDOCRINE ASSESSMENT

INTRODUCTION

Background

The essential role of membrane and intracellular receptors in human endocrine function has been firmly established and extensively studied (1). In animal models, much of the basic research into the mechanism of dioxin endocrine toxicity has focused on the dioxin-binding aryl hydrocarbon (Ah) receptor, which is superficially similar to endocrine receptors that mediate function of the thyroid, adrenal, and gonadal hormones. This receptor has been recently cloned and rapid progress can be expected in elucidating the taxonomy of this protein. Dioxin has been reported in previous studied to have several endrocrine effects. Although such receptors have not been isolated in human pancreatic (islet cell) tissue, one previous (2) and two recent (3,4) reports have raised the possibility that 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD, or dioxin) may be associated with impaired glucose metabolism.

As documented in previous (5-8) and more recent (9-13) animal studies, the thyroid is a target organ for TCDD toxicity though the mechanism is not clearly defined. Several reports have proved that dioxin-induced changes in thyroid indices (serum thyroxin [T_4], triiodothyronine [T_3] and thyroid stimulating hormone [TSH]) can be directionally different with definite species and strain specificity (12,13).

The finding in laboratory animals of physicochemical similarities between the dioxin-binding Ah and glucocorticoid (GRc) receptors (14,15) has prompted additional studies of the interaction of TCDD with other steroid hormones. Concern about the potential for harmful reproductive outcomes in humans, particularly veterans exposed to herbicides during the Vietnam War, has driven much of the basic research into the effects of dioxin on estrogen and androgen metabolism. A recent article provides a comprehensive summary of the extensive research into the developmental toxicity and teratogenicity of TCDD in laboratory animals (16).

In an early study, Kociba and colleagues defined the anti-estrogen effect of dioxin and documented a reduction in the incidence of estrogen-dependent uterine and mammary neoplasms in TCD-treated Long-Evans rats (17). Some of TCDD's estrogen-antagonistic effects appear to be mediated through the Ah receptor (18-20), while others mimic the action of progesterone (21,22). Additional studies (23,24), including recent experiments employing human breast cancer cell cultures (25-26), have implicated enzyme induction with accelerated estradiol metabolism as the basis for TCDD's estrogen-antagonistic effect.

Experimental studies have documented numerous adverse male reproductive effects in laboratory animals exposed to TCDD, including reduced testicular weight, impaired spermatogenesis, decreased testicular testosterone secretion, and atrophy of the androgen-

sensitive seminal vesicles and epididymis (27-30). Although TCDD administration is associated with diminished testicular testosterone secretion in rats (31,32), the mechanism is unclear and may involve the hypothalamic-pituitary axis. In rats, TCDD inhibits the secretion of luteinizing hormone (LH) by the pituitary gland, a reaction associated with androgen deficiency, and also inhibits the response of the pituitary to gonadotropin-releasing hormone (GnRH) secreted by the hypothalamus (33-35).

Other experiments have explored the effects of TCDD on the pituitary and the hypothalamus (36,37). The use of microsurgical techniques in female rats revealed that TCDD toxicity is aggravated by hypophysectomy, with a sparing effect noted upon administering either corticosterone or thyroid hormone (36). Another study defined a biochemical basis for the effect of TCDD on prolactin levels, controlled by the adenohypophysis in female rats (38).

The relevance of these experimental studies to endocrine disease in humans is uncertain, but the reports cited above (2-4) have raised the possibility that TCDD exposure is associated with altered glucose metabolism and an increased risk for diabetes. In the serum dioxin analyses of examination data collected in 1987-88 (4), Ranch Hand participants with the highest serum dioxin levels were nearly three times more likely to have elevated fasting blood sugar than were their Comparisons. Similarly, in a preliminary report from the National Institute for Occupational Safety and Health (NIOSH), an increased incidence of diabetes was found in workers exposed to dioxin (mean serum TCDD level of 220 ppt) versus unexposed controls (mean level of 7 ppt) (39).

Summary of Previous Analyses of the Air Force Health Study

1982 Baseline Study Summary Results

A comprehensive laboratory evaluation of the endocrine system was used for analysis in the Baseline examination in 1982. Five measures of endocrine status were assessed: T_3% uptake, T_4, free thyroxine index (FTI), testosterone, and 2-hour postprandial glucose.

Because technical capability did not exist to reliably perform serum dioxin evaluation in 1982, serum samples were collected and frozen for possible later analysis, but no models based on actual dioxin level were accomplished in 1982.

Results showed significant group differences for T_3% uptake (abnormally low), predominantly in Ranch Hands 40 years old or younger; the highest percentage of abnormalities was in those with high percent body fat. No group difference was noted for elevated 2-hour postprandial glucose values, and, as expected, the prevalence of abnormal values was associated with increased age and higher percent body fat. Lower testosterone values also were associated with increased age and higher percent body fat. Higher mean testosterone values (although still within normal range) were significantly more prevalent in the Ranch Hand group. Significant mean shifts were not noted for the T_3% uptake, T_4, and FTI variables.

These data, coupled with the animal literature on the profound influence of the endocrine system on lethality and body fat metabolism following TCDD exposure, clearly underscored the importance of evaluating the endocrine system more comprehensively, as in the subsequent followup examinations.

1985 Followup Study Summary Results

Questionnaire and review-of-systems data for past thyroid disease were essentially equivalent in both the Ranch Hand and Comparison groups. These historical data were confirmed by medical record reviews. Physical examination findings were necessarily limited to data from palpation of thyroid glands and testicles; the unadjusted results showed no significant group differences.

Evaluation of the endocrine system was conducted primarily by laboratory testing. The thyroid test battery consisted of $T_3\%$ uptake and TSH, as determined by radioimmunoassay (RIA) techniques. Testosterone, initial cortisol, differential cortisol (the difference between the initial and 2-hour cortisol levels), and 2-hour postprandial glucose levels also were analyzed. The $T_3\%$ uptake data showed no group differences for either mean values or frequency of abnormally low or high values. TSH results revealed a significantly higher mean level in the Ranch Hand group, but this difference was not detected by discrete analysis of the proportions of abnormally high TSH results.

The mean level of testosterone remained significantly elevated among Ranch Hands as contrasted with Comparisons in the 10 to 25 percent body fat category, but this difference was not reflected in the discrete analyses. For the few participants with less than 10 percent body fat (six Ranch Hands, four Comparisons), mean testosterone levels were lower for Ranch Hands than for Comparisons.

Two timed cortisol specimens showed no significant group differences in mean values and percent abnormalities. The difference between the timed cortisol results, termed the "differential cortisol," showed no significant group differences for non-Blacks or Blacks born before 1942, but Black Ranch Hands born in or after 1942 had a lower mean differential cortisol level than did their Comparisons.

Group means of 2-hour postprandial glucose levels were not statistically different, but discrete analyses revealed that there was a significantly higher frequency of glucose-impaired (at least 140 mg/dl, but less than 200 mg/dl) Comparisons than Ranch Hands. A constructed variable, comprising known diabetics and individuals classified as diabetic by the glucose tolerance test, showed no difference between the Ranch Hand and Comparison groups. As expected, past and current diabetes were highly influenced by the covariates age, race, and percent body fat.

1987 Followup Study Summary Results

The endocrinologic assessment did not disclose any statistically significant differences between the Ranch Hand and Comparison groups. The percentage of participants who indicated problems with current thyroid disease was similar between groups, as were the

percentages of thyroid and testicular abnormalities determined by palpation at the physical examination. Of the six laboratory examination variables examined—T_3% uptake, TSH, follicle stimulating hormone (FSH), testosterone, 2-hour postprandial glucose, and a composite diabetes indicator—the Ranch Hand TSH mean was marginally higher than the Comparison TSH mean, a finding that was statistically significant at the 1985 examination. Ranch Hand and Comparison mean levels for the other laboratory variables, including testosterone, were similar. For all laboratory variables, the percentage of Ranch Hands with abnormal values was higher than that of Comparisons with abnormal values, but none of these differences were statistically significant. Group differences for fasting glucose, analyzed in the gastrointestinal assessment, also were nonsignificant.

Serum Dioxin Analysis of 1987 Followup Study Summary Results

The endocrine assessment found a strong association between initial dioxin and an increase in diabetes and testes abnormalities. However, the analyses of current dioxin levels in Ranch Hands and Comparisons indicated that the increased risk was only apparent for Ranch Hands in the high current dioxin category (>33.3 ppt, n=187). These Ranch Hands also had significantly higher mean levels of TSH, fasting glucose, and 2-hour postprandial glucose than background Comparisons, as well as lower mean levels of T_3% uptake and testosterone. The discrete analyses of these variables found a significant increase in abnormally elevated fasting glucose levels and diabetic 2-hour postprandial glucose levels.

Parameters for the Endocrine Assessment

Dependent Variables

Questionnaire, physical examination, and laboratory data collected at the Air Force Health Study (AFHS) 1992 followup were used in the endocrine assessment. The self-reported information collected from the 1992 questionnaire were subsequently verified and analyses were based on the verified data.

Medical Records Data

The 1992 questionnaire posed a general screening question on thyroid function and disease. Each participant was asked during the face-to-face health interview, "Since the date of the last interview, has a doctor told you for the first time that you had thyroid problems?" All affirmative responses were verified by medical record review and added to physical examination data and previously reported and verified information on the thyroid function from the 1982 Baseline, the 1985 followup, and the 1987 followup for each participant. Based on the verified data, history of thyroid disease (interviewer-administered) was classified as "yes" or "no." Participants with a pre-SEA history of thyroid disease were excluded from the analysis of the history of thyroid disease variable.

Similar information was asked of each participant regarding diabetes. This information also was verified and combined with previous information. Participants with a verified history of diabetes were combined with those participants with a 2-hour postprandial glucose level of 200 mg/dl or greater at the 1992 physical examination and classified as "yes" for a

composite diabetes indicator variable. Those participants without a verified history of diabetes and with a 2-hour postprandial glucose level of less than 200 mg/dl at the 1992 physical examination were classified as "no." This composite diabetes indicator, derived from medical records review and laboratory results, was analyzed as part of the endocrine assessment. This variable also was used to distinguish diabetics from nondiabetics. The percentage of participants classified as diabetic at each of the examinations (1982, 1985, 1987, and 1992) are presented in the longitudinal analysis of the composite diabetes indicator (refer to Table 18-71).

As part of the 1992 questionnaire, questions were asked of diabetics regarding the use of insulin, oral diabetes medication, and diet. This self-reported information was verified and a diabetic severity index was constructed and analyzed for all participants. This index was categorized as "insulin dependent," "oral hypoglycemics," "diet only," or "no treatment" for diabetics and "no diabetes" for nondiabetics.

The date on which a participant was diagnosed with diabetes was used to create a time to diabetes onset variable, by determining the number of years between the date of diagnosis and the end date of the last time of duty in SEA. The number of years for those participants who have not been diagnosed with diabetes, which includes participants with a 2-hour postprandial glucose level of ≥ 200 mg/dl at the 1992 physical examination but not yet diagnosed with diabetes, is the number of years between the 1992 examination date and the end date of the last time of duty in SEA.

Participants with a pre-SEA history of diabetes were excluded from the analyses of the composite diabetes indicator, the diabetic severity variable, and the time to diabetes onset variable. Additionally, any participant who developed diabetes during his time of duty in SEA was excluded from the time to diabetes onset variable.

Physical Examination Data

The physical examination of the endocrine function included manual palpation of the thyroid gland and ultrasound techniques to determine testicular abnormalities. Thyroid abnormalities consisted of enlarged gland, tenderness, presence of nodules, or thyroidectomies. Ultrasound techniques for the assessment of abnormal testes and measurement of testicular volume are new to the AFHS for the 1992 followup and represent a major enhancement over previous cycles, which relied on a more subjective measure determined from manual palpation. Participants with pre-SEA history of thyroid disease or taking thyroid medication were excluded from the analysis of the thyroid gland. For the analysis of the testicular volume, participants with orchiectomies were excluded.

In addition, analyses restricted to diabetic participants were performed for several variables. Variables generated from the physical examination include retinopathy results, neuropathy results, and leg and peripheral Doppler pulse data (radial, femoral, popliteal, dorsalis pedis, posterior tibial, all leg, and all peripheral pulses). Pulse data based on all participants are analyzed in the cardiovascular assessment (see Chapter 15). Participants with pre-SEA diabetes were excluded from the analyses of these variables.

Laboratory Examination Data

For the 1992 followup, 14 laboratory variables were analyzed statistically in the endocrine assessment for all participants. TSH (μIU/ml), T_4 (μg/dl), LH (mIU/ml), and FSH (mIU/ml) were conducted by immunoassays based on chemiluminescence technology. Measurements for fasting glucose (mg/dl) were made using Paramax® equipment. Fasting urinary glucose analyses were conducted by accepted dipstick methods using a Clinitek 200® analyzer. Anti-thyroid antibodies, serum insulin (mIU/ml), serum glucagon (pg/ml), total testosterone (ng/dl), free testosterone (pg/ml), sex hormone binding globulin (nmol/l), and estradiol (pg/ml) were conducted by radioimmunoassay (RIA). An automated column chromatography analyzer was used to measure α-1-C hemoglobin (percent). An additional variable, the ratio of total testosterone to sex hormone binding globulin, also was analyzed.

Also, laboratory results for fasting glucose, fasting urinary glucose, serum insulin, serum glucagon, and α-1-C hemoglobin were analyzed separately for diabetics. Urinary protein, serum proinsulin (ng/ml), and serum C peptide (ng/ml) also were analyzed for diabetics only. Original plans were to analyze islet cell antibodies (present or absent) for diabetics, but no participant had islet cell antibodies present.

The Nichols Institute laboratory performed the serum proinsulin assays. Elevated serum proinsulin is often a result of insulinoma, a benign or malignant islet cell tumor of the pancreatic islets. The proteinuria measurement, while being an indicator of the renal function, is also important in the endocrine assessment because urinary protein is often present in diabetics.

Also, laboratory results for fasting glucose, fasting urinary glucose, serum insulin, serum glucagon, and α-1-C hemoglobin were analyzed with the analysis restricted to nondiabetics. In addition, the analyses of 2-hour postprandial glucose and 2-hour postprandial urinary glucose were restricted to nondiabetics only. Measurements for 2-hour postprandial glucose (mg/dl) were made using Paramax® equipment. Analyses for 2-hour postprandial urinary glucose were conducted by accepted dipstick methods using a Clinitek 200® analyzer. The 100-gram glucose load for the postprandial assays was standardized by the use of Glucola® and was not given to diabetics.

All laboratory variables were analyzed in both discrete and continuous forms except for anti-thyroid antibodies, fasting urinary glucose, 2-hour postprandial urinary glucose, urinary protein, sex hormone binding globulin, and the total testosterone to sex hormone binding globulin ratio. These variables were analyzed as discrete variables only. Sex hormone binding globulin and the total testosterone to sex hormone binding globulin ratio were categorized as "low" or "normal." The cutpoints for sex hormone binding globulin were based on Scripps Clinic and Research Facility (SCRF) reference values. For the total testosterone to sex hormone binding globulin ratio, "low" is defined as the 10th percentile of all data, because the clinical cutpoints have not been determined. Sex hormone binding globulin and the total testosterone to sex hormone binding globulin ratio only were analyzed as discrete variables due to the large percentage of sex hormone binding globulin measurements below the minimum level of detection. The other variables were dichotomized as "present" or "absent."

The cutpoints for the discrete analyses of other laboratory variables also were based on SCRF reference values. TSH, T_4, serum insulin, and serum C peptide were categorized as "abnormally low," "normal," and "abnormally high." However, due to sparse sample sizes, the "abnormally low" category was combined with the "normal" category for TSH and serum C peptide. For T_4, the "normal" and "abnormally high" categories were combined. The results for 2-hour postprandial glucose were coded as "normal" and "impaired." All other laboratory variables were dichotomized as "normal" or "abnormal" (abnormally high for all variables, except for total testosterone and free testosterone, which were classified according to abnormally low values).

Participants with thyroidectomies, a pre-SEA history of thyroid disease, or who are taking thyroid medication were excluded from the analyses of TSH, T_4, and anti-thyroid antibodies. For total and free testosterone, sex hormone binding globulin, and the total testosterone to sex hormone binding globulin ratio, participants with orchiectomies and those taking testosterone medication were excluded. Participants with pre-SEA diabetes were excluded from the analysis of fasting glucose, 2-hour postprandial glucose, fasting urinary glucose, 2-hour postprandial urinary glucose, serum insulin, serum glucagon, α-1-C hemoglobin, urinary protein, serum proinsulin, and serum C peptide. Due to a change in the preservative used to stabilize glucagon in blood samples, data from examination groups 68 to 81 were excluded from the analysis of the serum glucagon measurements. The batch of preservative purchased after group 67 was claimed, by the manufacturer, to be identical to the previous product, which was no longer available, but was later discovered to contain differences.

Covariates

The endocrine assessment includes the effects of the covariates age, race, and military occupation in the adjusted analyses of all variables. To adjust for the effects of stress on endocrinologic measures, personality type was an additional covariate for all variables except estradiol, luteinizing hormone, and FSH. Body fat was included in the adjusted analyses of all variables except the thyroid-related variables (past thyroid disease, thyroid gland abnormalities, TSH, T_4, and anti-thyroid antibodies), estradiol, luteinizing hormone, and FSH.

Age and body fat were treated as continuous variables for all adjusted analyses and categorized, as necessary, for interaction presentations. Personality type was determined from the Jenkins Activity Survey administered at the 1992 examination. This variable was derived from a discriminant function equation based on questions that best discriminate men judged to be Type A from those judged to be Type B (40). Positive scores reflected the Type A direction; negative scores reflected the Type B direction. This variable was dichotomized into Type A and Type B for all analyses.

Body fat, a measure of the relative body mass of an individual derived from height and weight recorded at the physical examination, was computed by the following formula (41).

$$Body\ Fat\ (in\ percent) = \frac{Weight\ (kg)}{[Height\ (m)]^2} \times 1.264 - 13.305.$$

In its discrete form, this variable was dichotomized as lean or normal (≤25%) and obese (>25%).

Each participant was asked in the 1992 questionnaire whether anyone in his immediate family ever had diabetes or sugar diabetes. A family history of diabetes covariate was constructed from this question and used in adjusted analyses of all diabetic-related dependent variables, including variables analyzed for diabetics only.

As described above, analyses restricted to diabetic participants were conducted for a number of dependent variables. For these analyses, a diabetic severity index was constructed and used as a covariate. This covariate was categorized as "insulin dependent," "oral hypoglycemics," "diet only," or "no treatment," and remained in the adjusted model throughout the stepwise model reduction.

The analyses of the pulse variables also were adjusted for lifetime cigarette smoking history, current cigarette smoking, lifetime alcohol history, current alcohol use, cholesterol, high-density lipoprotein (HDL), cholesterol-HDL ratio, family history of heart disease, and family history of heart disease before the age of 45, in the same manner as the analysis for the cardiovascular assessment (see Chapter 15). Based on the preliminary analyses in the cardiovascular assessment, the subset of these covariates used in the adjusted analyses were lifetime cigarette smoking history, current cigarette smoking, lifetime alcohol history, total cholesterol, HDL, and family history of heart disease.

Cutpoints for serum insulin, serum glucagon, serum proinsulin, and serum C peptide were dependent on whether the participant was fasting. Consequently, normal and abnormal levels for these variables were constructed according to a participant's laboratory value and fasting status at the physical examination. The fasting status-specific cutpoints are listed in Table 18-1. Additionally, a variable that designates a participant's fasting status was used in the continuous analyses of these variables.

Statistical Methods

Chapter 7, Statistical Methods, describes basic statistical methods used throughout this report. Table 18-1 summarizes the statistical analyses that were done for the endocrine assessment. The first part of this table describes the dependent variables and identifies the candidate covariates and the statistical methods. The second part of this table further describes the candidate covariates. Abbreviations used in the body of the table are defined at the end of the table. Dependent variable data were missing for some participants. The number of participants with missing data and those excluded due to medical reasons and pre-Southeast Asia (SEA) time of duty in SEA conditions are provided in Table 18-2.

Table 18-1.
Statistical Analyses for the Endocrine Assessment

Dependent Variables

Variable (Units)	Data Source	Data Form	Cutpoints	Candidate Covariates	Statistical Analyses
Past Thyroid Disease	MR-V	D	Yes No	AGE,RACE, OCC,PERS	U:LR,CS A:LR
Composite Diabetes Indicator	MR-V/ LAB	D	Yes (diabetic): Verified History or ≥200 mg/dl 2-hr. post-prandial glucose No: Otherwise	AGE,RACE, OCC,PERS, BFAT, FAMDIAB	U:LR,CS A:LR L:LR
Diabetic Severity	MR-V	D	Insulin Dependent Oral Hypoglycemics Diet Only No Treatment No Diabetes	AGE,RACE, OCC,PERS, BFAT, FAMDIAB	U:PR,CS A:PR
Time to Diabetes Onset (years)	MR-V/ LAB/ MIL	C	--	AGE,RACE, OCC,PERS, BFAT, FAMDIAB	U:GLM A:GLM
Thyroid Gland	PE	D	Abnormal Normal	AGE,RACE, OCC,PERS	U:LR,CS A:LR
Testicular Volume: Minimum (cm^3)	PE	C	--	AGE,RACE, OCC,PERS, BFAT	U:GLM,TT A:GLM
Testicular Volume: Total (cm^3)	PE	C	--	AGE,RACE, OCC,PERS, BFAT	U:GLM,TT A:GLM
Retinopathy Results (Diabetics only)	PE	D	Abnormal Normal	AGE,RACE, OCC,PERS, BFAT, FAMDIAB, DIABSEV	U:LR,CS A:LR
Neuropathy Results (Diabetics only)	PE	D	Abnormal Normal	AGE,RACE, OCC,PERS, BFAT, FAMDIAB, DIABSEV	U:LR,CS A:LR

Table 18-1. (Continued)
Statistical Analyses for the Endocrine Assessment

Dependent Variables

Variable (Units)	Data Source	Data Form	Cutpoints	Candidate Covariates	Statistical Analyses
Radial Pulses (Doppler) (Diabetics only)	PE	D	Abnormal Normal	AGE,RACE, OCC,PERS, BFAT, FAMDIAB, DIABSEV, PACKYR, CSMOK, DRKYR,ALC, CHOL,HDL, CHOL/HDL, HRTDIS, HRTDIS45	U:LR,CS A:LR
Femoral Pulses (Doppler) (Diabetics only)	PE	D	Abnormal Normal	AGE,RACE, OCC,PERS, BFAT, FAMDIAB, DIABSEV, PACKYR, CSMOK, DRKYR,ALC, CHOL,HDL, CHOL/HDL, HRTDIS, HRTDIS45	U:LR,CS A:LR
Popliteal Pulses (Doppler) (Diabetics only)	PE	D	Abnormal Normal	AGE,RACE, OCC,PERS, BFAT, FAMDIAB, DIABSEV, PACKYR, CSMOK, DRKYR,ALC, CHOL,HDL, CHOL/HDL, HRTDIS, HRTDIS45	U:LR,CS A:LR

Table 18-1. (Continued)
Statistical Analyses for the Endocrine Assessment

Dependent Variables

Variable (Units)	Data Source	Data Form	Cutpoints	Candidate Covariates	Statistical Analyses
Dorsalis Pedis Pulses (Doppler) (Diabetics only)	PE	D	Abnormal Normal	AGE,RACE, OCC,PERS, BFAT, FAMDIAB, DIABSEV, PACKYR, CSMOK, DRKYR,ALC, CHOL,HDL, CHOL/HDL, HRTDIS, HRTDIS45	U:LR,CS A:LR
Posterior Tibial Pulses (Doppler) (Diabetics only)	PE	D	Abnormal Normal	AGE,RACE, OCC,PERS, BFAT, FAMDIAB, DIABSEV, PACKYR, CSMOK, DRKYR,ALC, CHOL,HDL, CHOL/HDL, HRTDIS, HRTDIS45	U:LR,CS A:LR
Leg Pulses (Doppler) (Diabetics only)	PE	D	Abnormal Normal	AGE,RACE, OCC,PERS, BFAT, FAMDIAB, DIABSEV, PACKYR, CSMOK, DRKYR,ALC, CHOL,HDL, CHOL/HDL, HRTDIS, HRTDIS45	U:LR,CS A:LR

Table 18-1. (Continued)
Statistical Analyses for the Endocrine Assessment

Dependent Variables

Variable (Units)	Data Source	Data Form	Cutpoints	Candidate Covariates	Statistical Analyses
Peripheral Pulses (Doppler) (Diabetics only)	PE	D	Abnormal Normal	AGE,RACE, OCC,PERS, BFAT, FAMDIAB, DIABSEV, PACKYR, CSMOK, DRKYR,ALC, CHOL,HDL, CHOL/HDL, HRTDIS, HRTDIS45	U:LR,CS A:LR
Thyroid Stimulating Hormone (TSH) (μIU/ml)	LAB	D/C	Abnormal High: >5.5 Normal: ≤5.5	AGE,RACE, OCC,PERS	U:PR,CS,GLM, TT A:PR,GLM L:PR,GLM
Thyroxine (T_4) (μg/dl)	LAB	D/C	Abnormal Low: <4.8 Normal: ≥4.8	AGE,RACE, OCC,PERS	U:PR,CS,GLM, TT A:PR,GLM
Anti-Thyroid Antibodies	LAB	D	Present Absent	AGE,RACE, OCC,PERS	U:LR,CS A:LR
Fasting Glucose (mg/dl) (All participants)	LAB	D/C	Abnormal High: >115 Normal: ≤115	AGE,RACE, OCC,PERS, BFAT, FAMDIAB	U:LR,CS,GLM, TT A:LR,GLM L:LR,GLM
(Diabetics only)				AGE,RACE, OCC,PERS, BFAT, FAMDIAB, DIABSEV	U:LR,CS,GLM, TT A:LR,GLM
(Nondiabetics only)				AGE,RACE, OCC,PERS, BFAT, FAMDIAB	U:LR,CS,GLM, TT A:LR,GLM
2-Hour Postprandial Glucose (mg/dl) (Nondiabetics only)	LAB	D/C	Impaired: 140-<200 Normal: <140	AGE,RACE, OCC,PERS, BFAT, FAMDIAB	U:LR,CS,GLM, TT A:LR,GLM L:LR,GLM
Fasting Urinary Glucose (All participants)	LAB	D	Present Absent	AGE,RACE, OCC,PERS, BFAT, FAMDIAB	U:LR,CS A:LR

Table 18-1. (Continued)
Statistical Analyses for the Endocrine Assessment

Dependent Variables

Variable (Units)	Data Source	Data Form	Cutpoints	Candidate Covariates	Statistical Analyses
(Diabetics only)				AGE,RACE, OCC,PERS, BFAT, FAMDIAB, DIABSEV	U:LR,CS A:LR
(Nondiabetics only)				AGE,RACE, OCC,PERS, BFAT, FAMDIAB	U:Frequencies
2-Hour Postprandial Urinary Glucose (Nondiabetics only)	LAB	D	Present Absent	AGE,RACE, OCC,PERS, BFAT, FAMDIAB	U:LR,CS A:LR
Serum Insulin (mIU/ml) (All participants)	LAB	D/C	Abnormal Low: >18 (nonfast.) Normal: 18-56 (nonfast.) 0-30 (fasting) Abnormal High: >56 (nonfast.) >30 (fasting)	AGE,RACE, OCC,PERS, BFAT, FAMDIAB, FAST	U:PR,CS,GLM, TT A:PR,GLM
(Diabetics only)				AGE,RACE, OCC,PERS, BFAT, FAMDIAB, DIABSEV,FAST	U:PR,CS,GLM, TT A:PR,GLM
(Nondiabetics only)				AGE,RACE, OCC,PERS, BFAT, FAMDIAB, FAST	U:PR,CS,GLM, TT A:PR,GLM
Serum Glucagon (pg/ml) (All participants)	LAB	D/C	Abnormal High: >200 (nonfast.) >130 (fasting) Normal: ≤200 (nonfast.) ≤130 (fasting)	AGE,RACE, OCC,PERS, BFAT, FAMDIAB, FAST	U:LR,CS,GLM, TT A:LR,GLM

Table 18-1. (Continued)
Statistical Analyses for the Endocrine Assessment

Dependent Variables

Variable (Units)	Data Source	Data Form	Cutpoints	Candidate Covariates	Statistical Analyses
(Diabetics only)				AGE,RACE, OCC,PERS, BFAT, FAMDIAB, DIABSEV,FAST	U:LR,CS,GLM, TT A:LR,GLM
(Nondiabetics only)				AGE,RACE, OCC,PERS, BFAT, FAMDIAB, FAST	U:Frequencies, GLM,TT A:GLM
α-1-C Hemoglobin (percent) (All participants)	LAB	D/C	Abormal High: >7.3 Normal: ≤7.3	AGE,RACE, OCC,PERS, BFAT, FAMDIAB	U:LR,CS,GLM, TT A:LR,GLM
(Diabetics only)				AGE,RACE, OCC,PERS, BFAT, FAMDIAB, DIABSEV	U:LR,CS,GLM, TT A:LR,GLM
(Nondiabetics only)				AGE,RACE, OCC,PERS, BFAT, FAMDIAB	U:LR,CS,GLM, TT A:LR,GLM
Urinary Protein (Diabetics only)	LAB	D	Present Absent	AGE,RACE, OCC,PERS, BFAT, FAMDIAB, DIABSEV	U:LR,CS A:LR
Serum Proinsulin (ng/ml) (Diabetics only)	LAB-N	D/C	Abnormal High: >2.1 (nonfast.) >0.2 (fasting) Normal: ≤2.1 (nonfast.) ≤0.2 (fasting)	AGE,RACE, OCC,PERS, BFAT, FAMDIAB, DIABSEV,FAST	U:LR,CS,GLM, TT A:LR,GLM
Serum C Peptide (ng/ml) (Diabetics only)	LAB	D/C	Abnormal High: ≤5.6 (nonfast.) ≤4.0 (fasting) Normal: >5.6 (nonfast.) >4.0 (fasting)	AGE,RACE, OCC,PERS, BFAT, FAMDIAB, DIABSEV,FAST	U:PR,CS,GLM, TT A:PR,GLM

Table 18-1. (Continued)
Statistical Analyses for the Endocrine Assessment

Dependent Variables

Variable (Units)	Data Source	Data Form	Cutpoints	Candidate Covariates	Statistical Analyses
Total Testosterone (ng/dl)	LAB	D/C	Abnormal Low: <260 Normal: ≥260	AGE,RACE, OCC,PERS, BFAT	U:LR,CS,GLM, TT A:LR,GLM L:LR,GLM
Free Testosterone (pg/ml)	LAB	D/C	Abnormal Low: <16 (Age 40-49) <13 (Age 50-59) <11 (Age 60-69) <9 (Age ≥70) Normal: ≥16 (40-49) ≥13 (50-59) ≥11 (60-69) ≥9 (≥70)	AGE,RACE, OCC,PERS, BFAT	U:LR,CS,GLM, TT A:LR,GLM
Sex Hormone Binding Globulin (nmol/l)	LAB	D	Abnormal Low: <10 Normal: ≥10	AGE,RACE, OCC,PERS, BFAT	U:LR,CS A:LR
Total Testosterone to Sex Hormone Binding Globulin Ratio	LAB	D	Abnormal Low Normal	AGE,RACE, OCC,PERS, BFAT	U:LR,CS A:LR
Estradiol (pg/ml)	LAB	D/C	Abnormal High: >60 Normal: ≤60	AGE,RACE, OCC	U:LR,CS,GLM, TT A:LR,GLM
Luteinizing Hormone (LH) (mIU/ml)	LAB	D/C	Abnormal High: >5.9 Normal: ≤5.9	AGE,RACE, OCC	U:LR,CS,GLM, TT A:LR,GLM
Follicle Stimulating Hormone (FSH) (mIU/ml)	LAB	D/C	Abnormal High: >15 Normal: ≤15	AGE,RACE, OCC	U:LR,CS,GLM, TT A:LR,GLM

Table 18-1. (Continued)
Statistical Analyses for the Endocrine Assessment

Covariates

Variable (Abbreviation)	Data Source	Data Form	Cutpoints
Age (AGE)	MIL	D/C	Born ≥1942 Born <1942
Race (RACE)	MIL	D	Black Non-Black
Occupation (OCC)	MIL	D	Officer Enlisted Flyer Enlisted Groundcrew
Personality Type (PERS)	PE	D	A direction B direction
Body Fat (percent) (BFAT)	PE	D/C	Obese: >25% Lean or Normal: ≤25%
Family History of Diabetes (FAMDIAB)	Q-SR	D	Yes No
Diabetic Severity (DIABSEV)	MR-V	D	Insulin Dependent Oral Hypoglycemics Diet Only No Treatment
Lifetime Cigarette Smoking History (PACKYR) (pack-years)	Q-SR	D/C	0 >0-10 >10
Current Cigarette Smoking (CSMOK) (cigarettes/day)	Q-SR	D/C	0-Never 0-Former >0-20 >20
Lifetime Alcohol History (DRKYR) (drink-years)	Q-SR	D/C	0 >0-40 >40
Current Alcohol Use (ALC) (drinks/day)	Q-SR	D/C	0-1 >1-4 >4
Cholesterol (CHOL) (mg/dl)	LAB	D/C	≤200 >200-239 >240
High Density Lipoprotein (HDL) (mg/dl)	LAB	D/C	0-35 >35
Cholesterol-HDL Ratio (CHOL/HDL)	LAB	D/C	0-5 >5
Family History of Heart Disease (HRTDIS)	Q-SR	D	Yes No

Table 18-1. (Continued)
Statistical Analyses for the Endocrine Assessment

Covariates

Variable (Abbreviation)	Data Source	Data Form	Cutpoints
Family History of Heart Disease Before Age 45 (HRTDIS45)	Q-SR	D	Yes No
Fasting Status (FAST)	LAB	D	Yes No

Abbreviations

Data Source:	LAB	=	1992 laboratory results
	LAB-N	=	1992 Nichols Institute laboratory results
	MIL	=	Air Force military records
	MR-V	=	Medical records (verified)
	PE	=	1992 physical examination
	Q-SR	=	Health questionnaire (self-reported)
Data Form:	C	=	Continuous analysis only
	D	=	Discrete analysis only
	D/C	=	Discrete and continuous analyses for dependent variables; appropriate form for analysis (either discrete or continuous) for covariates
Statistical Analyses:	U	=	Unadjusted analyses
	A	=	Adjusted analyses
	L	=	Longitudinal analyses
Statistical Methods:	CS	=	Chi-square contingency table analysis (continuity-adjusted for 2x2 tables)
	GLM	=	General linear models analysis
	LR	=	Logistic regression analysis
	PR	=	Polychotomous logistic regression analysis
	TT	=	Two-sample t-test

Table 18-2.
Number of Participants with Missing Data for, or Excluded from, the Endocrine Assessment

		Group		Dioxin (Ranch Hands Only)		Categorized Dioxin	
Variable	Variable Use	Ranch Hand	Comparison	Initial	Current	Ranch Hand	Comparison
Composite Diabetes Indicator	DEP	3	5	2	3	3	4
Time to Diabetes Onset	DEP	0	1	0	0	0	1
Thyroid Gland	DEP	2	1	0	1	1	1
Testicular Volume	DEP	14	11	7	12	12	6
Diabetic Retinopathy[a]	DEP	1	1	0	1	1	1
Thyroid Stimulating Hormone (TSH)	DEP	0	1	0	0	0	0
Thyroxine (T_4)	DEP	0	1	0	0	0	0
Anti-Thyroid Antibodies	DEP	0	1	0	0	0	0
Fasting Glucose	DEP	0	1	0	0	0	0
2-Hour Postprandial Glucose[b]	DEP	1	2	0	1	1	1
Fasting Urinary Glucose	DEP	2	2	2	2	2	1
2-Hour Postprandial Urinary Glucose[b]	DEP	2	4	1	2	2	2
Serum Insulin	DEP	0	2	0	0	0	1
Serum Glucagon[c]	DEP	0	3	0	0	0	2
α-1-C Hemoglobin	DEP	0	1	0	0	0	0
Urinary Protein[a]	DEP	0	1	0	0	0	1
Serum Proinsulin[a]	DEP	8	7	5	8	8	6
Serum C Peptide[a]	DEP	8	7	5	8	8	6
Total Testosterone	DEP	0	1	0	0	0	0
Free Testosterone	DEP	0	1	0	0	0	0
Sex Hormone Binding Globulin	DEP	0	1	0	0	0	0

Table 18-2. (Continued)
Number of Participants with Missing Data for, or Excluded from, the Endocrine Assessment

		Group		Dioxin (Ranch Hands Only)		Categorized Dioxin	
Variable	Variable Use	Ranch Hand	Comparison	Initial	Current	Ranch Hand	Comparison
Total Testosterone to Sex Hormone Binding Globulin Ratio	DEP	0	1	0	0	0	0
Estradiol	DEP	0	1	0	0	0	0
Luteinizing Hormone	DEP	0	1	0	0	0	0
Follicle Stimulating Hormone	DEP	0	1	0	0	0	0
Personality Type	COV	1	1	1	1	1	1
Lifetime Alcohol History[a]	COV	3	3	3	3	3	3
Current Alcohol Use[a]	COV	3	3	3	3	3	3
High Density Lipoprotein[a]	COV	5	8	3	5	5	6
Cholesterol-HDL Ratio[a]	COV	5	8	3	5	5	6
Family History of Heart Disease[a]	COV	2	1	0	2	2	0
Family History of Heart Disease Before Age 45[a]	COV	6	6	3	6	6	4
Diabetes	EXC	144	182	98	140	140	151
Pre-SEA Diabetes	EXC	2	3	2	2	2	3
Pre-SEA Thyroid Disease	EXC	7	6	4	7	7	6
Thyroid Medication	EXC	16	33	9	16	16	27
Thyroidectomy	EXC	8	14	3	8	8	11
Testosterone Medication	EXC	7	5	0	6	6	4
Orchiectomy	EXC	9	4	5	9	9	3

Table 18-2. (Continued)
Number of Participants with Missing Data for, or Excluded from, the Endocrine Assessment

		Group		Dioxin (Ranch Hands Only)		Categorized Dioxin	
Variable	Variable Use	Ranch Hand	Comparison	Initial	Current	Ranch Hand	Comparison
Examination Groups 68-81 (Exclusion for Glucagon)	EXC	123	172	66	104	104	102

[a]Missing data for diabetics only.
[b]Missing data for nondiabetics only.
[c]Missing data for examination groups 1-67.

Abbreviations: DEP = Dependent variable (missing data).
COV = Covariate (missing data).
EXC = Exclusion.

Note: 952 Ranch Hands and 1,281 Comparisons;
520 Ranch Hands for initial dioxin; 894 Ranch Hands for current dioxin;
894 Ranch Hands and 1,063 Comparisons for categorized dioxin.
One Ranch Hand missing total lipids for current dioxin.

Cutpoints for free testosterone are age-dependent. Consequently, normal and abnormal levels for free testosterone were constructed according to a participant's laboratory value and age at the physical examination. The age-specific cutpoints are listed in Table 18-1, and the reference ages for these cutpoints are given in parentheses following the cutpoints.

The analysis of time to diabetes onset utilized statistical failure time (or survival time) models, whereby a time to diabetes onset was estimated for participants who have not developed diabetes. The failure time analysis incorporates the actual time to diabetes onset for diabetics and participants diagnosed as diabetic at the 1992 examination and extrapolates the time at which diabetes would occur for nondiabetics. Further details on the statistical methods used for analysis of time to diabetes onset are discussed in Chapter 7, Statistical Methods.

Analyses restricted to diabetics were done for specific variables listed in Table 18-1. These analyses evaluated whether the association between exposure and the dependent variable changes depending on the level of diabetic severity for diabetic participants. Analyses restricted to nondiabetic participants also are specified in Table 18-1.

Analyses of data collected at the 1987 followup study indicated that dioxin was associated with military occupation. In general, enlisted personnel had higher levels of dioxin than officers, with enlisted groundcrew having higher levels than enlisted flyers. Consequently, adjustment for military occupation in statistical models using dioxin as a measure of exposure may improperly mask an actual dioxin effect. However, occupation also can be a surrogate for socioeconomic effects. Failure to adjust for occupation could overlook important risk factors related to lifestyle. If occupation was found to be significantly associated with a dependent variable in the 1992 followup analyses and was retained in the final statistical models using dioxin as a measure of exposure, the dioxin effect was evaluated in the context of two models. Analyses were performed with and without occupation in the final models to investigate whether conclusions regarding the association between the health endpoint and dioxin differed.

Similarly, dioxin exhibited a significant positive association with body fat, cholesterol, and HDL, in the serum dioxin analysis of the 1987 followup data, and these associations also are seen in the 1992 followup analyses (see Chapter 8). Body fat, and cholesterol and HDL for the Doppler pulse measurements, are risk factors for the endocrine health endpoints which must be introduced to the adjusted model; however, adjusting for these covariates has the potential to over-adjust the model for the effects of dioxin exposure. To investigate the effects of adjustment, when these covariates were found to be significantly associated with a dependent variable and retained in the final model, the dioxin effect was evaluated in the context of two models. Analyses again were performed with and without these covariates in the model to investigate whether conclusions regarding the associations between the health endpoint and dioxin differed.

The results of the analyses without occupation, body fat, cholesterol, and HDL in the final adjusted model are presented in Appendix N-3 and are discussed in the text only if the level of significance differs from the original final adjusted model (significant versus nonsignificant).

Longitudinal Analyses

Longitudinal analyses were performed for the composite diabetes indicator, TSH, fasting glucose, 2-hour postprandial glucose, and total testosterone to assess if exposure and the changes in these variables between the 1992 examination and previous examinations are associated. Longitudinal analyses were conducted on both the continuous and discrete forms of TSH, fasting glucose, 2-hour postprandial glucose, and total testosterone. Discrete longitudinal analyses were performed on the composite diabetes indicator.

RESULTS

Dependent Variable-Covariate Associations for the Endocrine Assessment

Tests of covariate associations found past thyroid disease to be highly associated with age (Appendix Table N-1-1: $p=0.009$). For participants born in or after 1942, 4.0 percent reported a history of thyroid disease compared to 6.6 percent of participants born before 1942.

The results of the tests of covariate associations for the composite diabetes indicator revealed all candidate covariates except occupation and race to be statistically significant. The association between the composite diabetes indicator and race was marginally significant. The analysis of age showed that 8.2 percent of young participants and 19.1 percent of older participants were diabetic ($p<0.001$). For Black participants, 19.9 percent were diabetic, while only 14.1 percent of non-Black participants were diabetic ($p=0.091$). The analysis of personality type revealed that 12.2 percent of Type A participants and 16.1 percent of Type B participants had diabetes ($p=0.012$). Covariate analyses showed body fat to be highly associated with the composite diabetes indicator ($p<0.001$) with more than twice as many diabetics in the obese category (26.1 percent) than in the lean or normal category (10.4 percent). For participants who reported a family history of diabetes, 21.9 percent were diabetic compared to only 12.0 percent of participants who did not report a family history of diabetes ($p<0.001$).

Age, race, personality type, body fat, and family history of diabetes were significant in the covariate analyses for diabetic severity. In the analysis of age, the percentages of younger participants who used no treatment, diet, oral hypoglycemics, and insulin to treat their condition were 5.1, 1.8, 0.9, and 0.3 respectively. For older participants, these percentages were 11.0, 3.5, 2.5, and 2.0 respectively ($p<0.001$). The analysis of race showed that for Black participants, 13.0 used no treatment, 0.8 percent used diet as a form of treatment, 4.6 percent used oral hypoglycemics, and 1.5 percent used insulin. The percentages of non-Black participants who employed no treatment, diet, oral hypoglycemics, and insulin were 8.2, 2.9, 1.7, and 1.3 respectively ($p=0.021$). Covariate analyses revealed that 15.9 percent, 4.8 percent, 3.9 percent, and 1.6 percent of obese participants utilized no treatment, diet, oral hypoglycemics, and insulin respectively to treat their disorder while 6.0 percent, 2.1 percent, 1.1 percent, and 1.2 percent of lean or normal participants respectively, used these methods in the treatment of diabetes ($p<0.001$). Of the participants with a family history of diabetes, 10.9 used no treatment and 4.8 percent used diet as a form of treatment, compared to 7.5 percent and 2.2 percent for participants without a family history of diabetes. In addition, 3.8 percent and 2.3 percent of diabetic participants with a family history of diabetes used oral

hypoglycemics or insulin for treatment in contrast to 1.3 percent and 1.0 percent for those participants without a family history of diabetes ($p<0.001$). The analysis of personality type showed, for Type A participants, 7.0 percent, 2.7 percent, 1.6 percent, and 1.0 percent used no treatment, diet only, oral hypoglycemics, or insulin respectively. For Type B participants, these percentages were 9.6, 2.8, 2.0, and 1.6 respectively ($p=0.098$).

Covariate association analyses of time to diabetes onset utilized statistical failure time models to incorporate the actual time to diabetes onset, from time of duty in SEA, for diabetics and to estimate the time at which diabetes would occur for nondiabetics. Further details on the statistical methods used for analysis of time to diabetes onset are discussed in Chapter 7, Statistical Methods.

Time to diabetes onset was significantly associated with age ($p<0.001$), personality type ($p=0.027$), body fat ($p<0.001$), and family history of diabetes ($p<0.001$) and was marginally associated with race ($p=0.069$). Older participants developed diabetes sooner after time of duty in SEA than did younger participants. The number of years to develop diabetes after time of duty in SEA was shorter for Blacks than for non-Blacks. Type A participants tended to develop diabetes longer after time of duty in SEA than Type B participants. Obese participants developed diabetes sooner after time of duty in SEA than did lean or normal participants. Similarly, participants with a family history of diabetes developed diabetes sooner after the time of duty in SEA than did participants without a family history of diabetes.

Minimum testicular volume was shown to be highly associated with both age and race in the tests of covariate association ($p<0.001$ for both covariates). In the analysis of age, the correlation coefficient between minimum testicular volume and age was -0.153. For Black and non-Black participants, average minimum testicular volumes were 14.30 cm^3 and 16.02 cm^3 respectively.

The results of the tests of covariate association for total testicular volume paralleled those for minimum testicular volume. The analysis of age displayed a negative correlation with total testicular volume ($r=-0.140$, $p<0.001$). Mean total testicular volume for Blacks was 30.55 cm^3 compared to 34.20 cm^3 for non-Blacks ($p<0.001$).

Covariate tests of association for retinopathy revealed diabetic severity and family history of diabetes to be significant ($p<0.001$ and $p=0.025$ respectively). Of the participants who employed no form of treatment for their diabetes, 0.5 percent had retinopathy. Of the diabetic participants who relied on diet, oral hypoglycemics, or insulin, the percentages with retinopathy were 3.3, 7.3, and 21.4 respectively. In the analysis of family history of diabetes, 7.1 percent of the participants who reported a family history of diabetes had retinopathy compared to only 1.5 percent of those who did not have a history of diabetes in their families.

Neuropathy results was highly associated with diabetic severity in the covariate tests of association ($p<0.001$). For participants who treated their diabetes with insulin, 44.8 percent had neuropathy, compared to 17.1 percent who used oral hypoglycemics and 3.2 percent who relied on diet alone. Of the diabetic participants who used no treatment for their disorder, 3.7 percent had neuropathy.

Both diabetic severity and current cigarette smoking were significantly associated with femoral pulses in the covariate analyses ($p=0.090$ and $p<0.001$ respectively). In the analysis of diabetic severity, 2.7 percent of the diabetics who did not treat their diabetic condition had abnormal femoral pulses. Of those who treated their diabetes, the percentages with abnormal femoral pulses were 10.3, 0.0, and 3.2 for insulin, oral hypoglycemics, and diet respectively. In the analysis of current cigarette smoking, no abnormal femoral pulses were found in diabetics who had never smoked, whereas 1.2 percent of diabetics who had formerly smoked had abnormal femoral pulses. Of the participants who smoked 0-20 cigarettes per day, 12.8 percent had abnormal femoral pulses compared to 6.3 percent for those who smoked more than 20 cigarettes daily.

In the covariate tests of association for popliteal pulses, diabetic severity and current cigarette smoking were highly significant covariates ($p=0.002$ and $p<0.001$ respectively). The analysis of diabetic severity found that 2.7 percent of diabetic participants who used no treatment for their condition had abnormal popliteal pulses. Of the diabetics who relied on diet alone, 3.2 percent had abnormal popliteal pulses compared to 2.4 percent of those who used oral hypoglycemics. Of the insulin-dependent participants, 17.2 percent had abnormal popliteal pulses. In the analysis of current cigarette smoking, no abnormal popliteal pulses were seen for diabetics who had never smoked, whereas for former smokers, 1.2 percent had abnormal popliteal pulses. For diabetics who smoked either 0 to 20 cigarettes per day, or more than 20 cigarettes per day, the percentages with abnormal popliteal pulses were 17.0 and 9.4 respectively.

Covariate tests of association found the associations of dorsalis pedis pulses with age, diabetic severity, family history of heart disease, current cigarette smoking, lifetime cigarette smoking history, and lifetime alcohol history to be significant or marginally significant. In the analysis of age, 16.5 percent of diabetics born before 1942 had abnormal dorsalis pedis pulses compared to 7.7 percent for those born in or after 1942 ($p=0.082$). The analysis of diabetic severity showed that 11.6 percent of the participants who did not use a form of diabetic treatment had abnormal dorsalis pedis pulses, whereas diabetics who used insulin, oral hypoglycemics, or diet for treatment had 31.0, 17.1, and 12.9 percent abnormal dorsalis pedis pulses ($p=0.045$). For family history of heart disease, covariate tests revealed that 18.7 percent of the diabetics who had no history of heart disease in their families had abnormal dorsalis pedis pulses compared to only 11.2 percent for the diabetics who did report a family history of the disease ($p=0.083$). In the analysis of current cigarette smoking, 6.9 percent of the diabetics who never smoked had abnormal dorsalis pedis pulses, while 13.0 percent of those who were former smokers had abnormal pulses. Of the diabetics who currently smoke either 0 to 20 cigarettes per day or more than 20 cigarettes per day, 27.7 and 18.8 percent respectively had abnormal dorsalis pedis pulses ($p=0.012$). The analysis of lifetime cigarette smoking history found that 6.9 percent of non-smokers possessed abnormal dorsalis pedis pulses compared to 9.8 and 19.9 percent for participants with between 0 and 10 pack-years and more than 10 pack-years ($p=0.012$). Covariate analyses showed that for diabetics with a lifetime alcohol history of either 0 drink-years, 0 to 40 drink-years, or more than 40 drink-years, the percentages with abnormal dorsalis pedis pulses were 4.2, 12.1, and 20.8 respectively ($p=0.044$).

Posterior tibial pulses was found to be significantly related to age, diabetic severity, current cigarette smoking, and lifetime cigarette smoking history in the covariate tests of association. Of the older diabetics, 9.5 percent had abnormal posterior tibial pulses in contrast to only 1.3 percent of the younger diabetics (p=0.032). In the analysis of diabetic severity, 6.9 percent of the participants who did not treat their diabetic condition possessed abnormal posterior tibial pulses. Of the participants who treated their diabetes with diet, oral hypoglycemics, or insulin, 3.2, 7.3, and 20.7 percent had abnormal posterior tibial pulses, (p=0.029). Covariate tests revealed that non-smokers did not have abnormal posterior tibial pulses, whereas 6.5 percent of former smokers had abnormal pulses. For those who presently smoke either 0 to 20 cigarettes per day or more than 20 cigarettes per day, 19.2 and 12.5 percent had abnormal posterior tibial pulses (p=0.001). For diabetics with a lifetime cigarette smoking history of 0 pack-years, 0 to 10 pack-years, and more than 10 pack-years, the percentages with abnormal posterior tibial pulses were 0.0, 6.1, and 11.5 respectively.

Covariate analyses showed that leg pulses were significantly associated with age, diabetic severity, family history of heart disease, current cigarette smoking, lifetime cigarette smoking history, and lifetime alcohol history. In the analysis of age, 18.1 percent of older diabetics and 7.7 percent of younger diabetics had abnormal leg pulses (p=0.043). The analysis of diabetic severity showed that of the diabetics who did not treat their condition, 13.2 percent had abnormal leg pulses. For those who used insulin, oral hypoglycemics, or diet in the treatment of their diabetes, 31.0, 19.5, and 12.9 percent had abnormal leg pulses (p=0.076). Of the diabetics who reported a family history of heart disease, 11.7 percent had abnormal leg pulses in contrast to 20.9 percent of those who did not cite a history of the disease in their families (p=0.039). In the analysis of current cigarette smoking, 6.9 and 14.2 percent of the non-smokers and former smokers had abnormal leg pulses. For those who currently smoke 0 to 20 cigarettes per day and more than 20 cigarettes per day, 29.8 and 21.9 percent had abnormal leg pulses (p=0.005). Of the diabetics who have never smoked, 6.9 percent had abnormal leg pulses compared to 11.0 and 22.3 percent for those with a history of cigarette smoking 0 to 10 pack-years and more than 10 pack-years (p=0.006). The analysis of lifetime alcohol history showed that the percentages of diabetics with abnormal leg pulses were 4.2, 12.6, and 22.8 for the categories of 0 drink-years, 0 to 40 drink-years, and more than 40 drink-years (p=0.021).

Significant associations between peripheral pulses and age, diabetic severity, family history of heart disease, current cigarette smoking, lifetime cigarette smoking history, and lifetime alcohol history were evident from the covariate tests of association. Of the diabetics born before 1942, 18.9 percent had abnormal peripheral pulses in contrast to 7.7 percent of those born in or after 1942 (p=0.030). The analysis of diabetic severity found that 13.8 percent of the diabetics who did not treat their condition had abnormal peripheral pulses. Diabetics who used diet only, oral hypoglycemics, or insulin to treat their condition had 12.9, 22.0, and 31.0 percent abnormal peripheral pulses (p=0.071). Of the diabetics without a history of heart disease in their family, 20.9 percent had abnormal peripheral pulses compared to only 12.9 percent for those with a family history of heart disease (p=0.078). In the analysis of current cigarette smoking, 8.2 percent of non-smokers and 14.8 percent of former smokers had abnormal peripheral pulses whereas 29.8 and 21.9 percent of diabetics smoking between 0 and 20 and over 20 cigarettes per day had abnormal peripheral pulses (p=0.013). The analysis of lifetime cigarette smoking history showed that for the categories of 0 pack-

years, either 0 to 10 pack-years, or more than 10 pack-years, 8.2, 11.0, and 22.3 percent of the diabetic participants had abnormal peripheral pulses (p=0.008). Of the diabetics with a lifetime alcohol history of 0 drink-years, 4.2 percent had abnormal peripheral pulses whereas for those with a history of either 0 to 40 drink-years or more than 40 drink-years, 13.7 and 22.8 percent had abnormal pulses (p=0.034).

Covariate analyses showed that thyroid stimulating hormone in its continuous form was significantly associated with age, race, and occupation. The correlation coefficient between age and TSH was 0.088 (p<0.001). For Black participants, the mean TSH was 1.19 mIU/ml compared to 1.62 mIU/ml for non-Black participants (p<0.001). For officers, enlisted flyers, and enlisted groundcrew, average TSH was 1.68, 1.49, and 1.56 mIU/ml respectively (p=0.003). For TSH in its discrete form, covariate analysis revealed that age was the only significant covariate (p=0.077). For participants born before 1942, 2.9% had an abnormally high TSH measurement in contrast to 1.7% for participants born in or after 1942.

Occupation was the only covariate significantly associated with thyroxine in both its discrete and continuous forms in the covariate analyses. For thyroxine measured continuously, mean levels of thyroxine for officers, enlisted flyers, and enlisted groundcrew were 7.57 mg/dl, 7.96 mg/dl, and 7.98 mg/dl (p=0.001). Analysis of thyroxine in its discrete form revealed that 0.3 percent of both enlisted flyers and enlisted groundcrew had abnormally low thyroxine levels compared to 1.2 percent for officers (p=0.040).

For fasting glucose in its continuous form, covariate analyses involving all participants found that age, race, personality type, body fat, and family history of diabetes were significant. In the analysis of age, the correlation coefficient with fasting glucose was 0.191 (p<0.001). The correlation coefficient between body fat and fasting glucose was 0.209 (p<0.001). The mean fasting glucose level for Blacks was 109.06 mg/dl in contrast to 104.03 mg/dl for non-Blacks (p=0.008). The analysis of personality type revealed that mean fasting glucose for Type A participants was 103.43 mg/dl, while mean fasting glucose for Type B participants was 105.00 mg/dl. For participants reporting a family history of diabetes, the mean fasting glucose was 108.12 mg/dl compared to 103.21 mg/dl for those participants who did not have a family history of the disease (p<0.001).

Age, race, personality type, body fat, and family history of diabetes also were significantly associated with fasting glucose in the discrete form. The analysis of age revealed that 17.8 percent of the participants born before 1942 had abnormally high fasting glucose compared to only 7.0 percent for participants born in or after 1942 (p<0.001). For race, the percentages of participants with abnormally high fasting glucose levels were 21.4 percent for Blacks and 12.7 percent for non-Blacks (p=0.007). Of the participants with a Type A personality, 11.4 percent had abnormal fasting glucose compared to 14.6 percent of the participants with a Type B personality (p=0.031). The analysis of body fat revealed that 23.1 percent of the participants with an elevated body fat had abnormally high fasting glucose, while only 9.8 percent of lean or normal participants had abnormal fasting glucose (p<0.001). For participants with a family history of diabetes, 18.2 percent had abnormally high fasting glucose whereas 11.6 percent of the participants without a family history of diabetes had abnormal fasting glucose (p<0.001).

Covariate analyses using diabetic participants only revealed that race and diabetic severity were significantly associated with fasting glucose in its continuous form. For Black participants, mean fasting glucose was 160.58 mg/dl, while for non-Blacks, mean fasting glucose was 140.48 mg/dl ($p=0.058$). In the analysis of diabetic severity, mean fasting glucose was 130.64 mg/dl for diabetics not treating their diabetes. For participants treating their diabetes with diet only, oral hypoglycemics, or insulin, mean fasting glucose was 141.57 mg/dl, 187.22 mg/dl, and 166.60 mg/dl respectively ($p<0.001$). In the covariate analyses for diabetics only, age and diabetic severity also were significant for fasting glucose in its discrete form. Of the diabetics born before 1942, 72.4 percent had abnormally high fasting glucose compared to 59.0 percent of the diabetics born in or after 1942 ($p=0.036$). For the diabetic severity analyses, the percentages of diabetics using no treatment, diet only, oral hypoglycemics, or insulin were 64.6, 61.3, 92.7, and 82.8 respectively ($p=0.001$).

In the covariate analyses involving only nondiabetic participants, age, occupation, personality type, and body fat were significantly associated with fasting glucose measured continuously. For the analyses of age and body fat, the respective correlation coefficients were 0.169 and 0.165 ($p<0.001$ for both covariates). The analysis of occupation showed that mean fasting glucose for officers and enlisted flyers were 99.51 mg/dl and 99.60 mg/dl compared to 98.43 mg/dl for enlisted groundcrew ($p=0.021$). For nondiabetics with a Type A personality, mean fasting glucose was 98.64 mg/dl in contrast to 99.36 mg/dl for Type B participants ($p=0.068$). For nondiabetic participants, covariate tests of association for fasting glucose in its discrete form found age to be the only significant covariate. The percentages of abnormalities were 5.0 percent for nondiabetics born before 1942 and 2.4 percent for those born in or after 1942.

With the exception of race, all candidate covariates were significantly associated with discrete and continuous 2-hour postprandial glucose. For continuous 2-hour postprandial glucose, the respective correlation coefficients for age and body fat were 0.188 ($p<0.001$) and 0.265 ($p<0.001$). For officers and enlisted groundcrew, mean 2-hour postprandial glucose levels were 102.17 mg/dl and 103.31 mg/dl in contrast to 107.66 mg/dl for enlisted flyers ($p=0.018$). Average 2-hour postprandial glucose for nondiabetics with a Type A personality was 100.89 mg/dl compared to 105.61 mg/dl for those with a Type B personality ($p<0.001$). For family history of diabetes, mean 2-hour postprandial glucose levels were 108.53 mg/dl for nondiabetics with a family history of diabetes and 102.46 mg/dl for nondiabetics without a family history of diabetes ($p<0.001$). Covariate analyses between discrete 2-hour postprandial glucose and age revealed that 16.8 percent of nondiabetics born before 1942 had an impaired 2-hour postprandial glucose level compared to only 8.9 percent for those born in or after 1942 ($p<0.001$). For officers, enlisted flyers, and enlisted groundcrew, the percentages of nondiabetics with an impaired level of 2-hour postprandial glucose were 11.1 percent, 15.8 percent, and 14.1 percent respectively ($p=0.075$). Of the nondiabetics with a Type A personality, 10.4 percent had an impaired level of 2-hour postprandial glucose in contrast to 15.3 percent for those with a Type B personality ($p=0.003$). The analysis of body fat showed that 23.2 percent of obese nondiabetics had an impaired level of 2-hour postprandial glucose whereas, for lean or normal nondiabetics, only 10.4 percent had an impaired level ($p<0.001$). For nondiabetics with a family history of diabetes, 17.0 percent had impaired 2-hour postprandial glucose compared to only 12.1 percent for those without a family history of the disorder ($p=0.014$).

Significant covariates disclosed in the covariate analysis of fasting urinary glucose for all participants included age, race, body fat, and family history of diabetes. In the analysis of age, 4.2 percent of participants born before 1942 had fasting urinary glucose present in contrast to only 1.6 percent for those born in or after 1942 ($p=0.001$). The analysis of race showed that 6.1 percent of Blacks and 2.9 percent of non-Blacks had fasting urinary glucose present ($p=0.068$). For obese participants, 6.0 percent had fasting urinary glucose present compared to only 2.1 percent for lean or normal participants ($p<0.001$). For participants with a family history of diabetes, 4.8 percent had fasting urinary glucose present compared to only 2.5 percent for those with no family history of diabetes ($p=0.010$).

Diabetic severity was the only covariate significantly associated with fasting urinary glucose in the covariate analysis restricted to diabetics. The analysis of diabetic severity found that 11.7 percent of the diabetics who did not treat their diabetes had fasting urinary glucose present. Of the diabetics who used diet, oral hypoglycemics, or insulin to treat their diabetes, 21.0 percent, 43.9 percent, and 48.3 percent had fasting urinary glucose present ($p<0.001$).

Restricted to nondiabetics, there was only one participant, a Comparison, with abnormal fasting urinary glucose. Therefore, tests of covariate association were not performed for this variable for the nondiabetic cohort.

Covariate analysis revealed that both age and occupation were significantly associated with 2-hour postprandial urinary glucose. In the analysis of age, 20.5 percent of nondiabetics born before 1942 had 2-hour postprandial urinary glucose present while only 15.9 percent of those born in or after 1942 had 2-hour postprandial glucose present ($p=0.012$). For officers, enlisted flyers, and enlisted groundcrew, the percentages with 2-hour postprandial urinary glucose present were 14.3, 21.8, and 20.9 respectively ($p=0.001$).

Serum insulin in its continuous form increased with age ($p<0.001$) and body fat ($p<0.001$). Black participants had lower serum insulin levels than non-Black participants ($p=0.048$). Participants with Type A personalities had lower serum insulin levels than participants with Type B personalities ($p<0.001$). The analysis of diabetic participants revealed that mean serum insulin levels increased as body fat increased ($p<0.001$). The Black diabetics had lower mean serum insulin levels than the non-Black diabetics ($p=0.001$). Diabetic participants with a family history of diabetes had lower serum insulin levels than diabetic participants with no family history of diabetes ($p=0.030$). Diabetic participants who are insulin dependent had the highest mean serum insulin levels followed by participants not treating their diabetes, participants using oral hypoglycemics, and participants who control their diabetes through diet only ($p<0.001$). Analysis of nondiabetic participants showed mean serum insulin levels increased with age ($p<0.001$) and body fat ($p<0.001$). Nondiabetic enlisted flyers had the highest mean serum insulin levels followed by the enlisted groundcrew then the officers ($p=0.003$). Nondiabetic participants with personality Type A had lower mean serum insulin levels than those with personality Type B ($p<0.001$). Nondiabetic participants with a family history of diabetes had higher serum insulin levels than those participants with no family history of diabetes ($p=0.002$).

Serum insulin, when categorized as abnormally low, normal, or abnormally high, revealed that the percentage of participants with low serum insulin levels decreased with age and the percentage of participants with high serum insulin levels increased with age ($p<0.001$). The percentage of participants with abnormally low serum insulin levels increased as body fat decreased and the percentage of participants with abnormally high serum insulin levels decreased as body fat decreased ($p<0.001$). A greater percentage of participants with low serum insulin levels had Type A personalities whereas a greater percentage of participants with high serum insulin levels had Type B personalities ($p<0.001$). The percentage of diabetic participants with abnormally low serum insulin levels increased as body fat increased and the percentage of diabetic participants with abnormally high serum insulin levels decreased as body fat increased ($p=0.017$). In both the abnormally low and abnormally high strata, a greater percentage of diabetic participants had Type B personalities than Type A personalities ($p=0.030$). A higher percentage of diabetic participants with abnormally low serum insulin levels were Black, whereas a greater percentage of diabetic participants with abnormally high serum insulin levels were non-Black ($p<0.001$). The low serum insulin category contained only diabetic enlisted flyers. No abnormally low serum insulin levels were noted for the diabetic officers and diabetic enlisted groundcrew. The high serum insulin category contained a greater percentage of diabetics who are insulin dependent followed by diabetic enlisted groundcrew and diabetic enlisted flyers ($p=0.003$). The low serum insulin category contained only insulin dependent diabetics. The high serum insulin category contained a greater percentage of insulin dependent diabetics followed by participants not treating their diabetes, participants who are treating their diabetes with oral hypoglycemics, and participants who are treating their diabetes with diet only ($p<0.001$). Analysis of the nondiabetic cohort showed the percentage of participants with low serum insulin decreased with age and the percentage of participants with high serum insulin increased with age ($p<0.001$). The percentage of nondiabetic participants in the abnormally low strata increases as body fat increases. The percentage of nondiabetic participants in the abnormally high strata decreases as body fat increases ($p<0.001$).

The low serum insulin category contained a greater percentage of officers followed by enlisted groundcrew and then enlisted flyers. The high serum insulin category contained a greater percentage of enlisted flyers followed by enlisted groundcrew and then officers ($p=0.018$). In both the abnormally low and abnormally high serum insulin strata, a higher percentage of nondiabetic participants had personality Type B than Type A ($p=0.003$). A greater percentage of nondiabetic participants in the abnormally low serum insulin strata did not have a family history of diabetes. A greater percentage of nondiabetic participants in the abnormally high serum insulin strata had a family history of diabetes ($p=0.013$).

Serum glucagon in its continuous form increased with age ($p<0.001$) and body fat ($p<0.001$) for all participants. The analysis of diabetic participants revealed that those who control their diabetes through diet only had the highest mean serum glucagon levels followed by participants who did not treat their diabetes, participants who use oral hypoglycemics, and participants who are insulin dependent ($p<0.001$). Analysis of nondiabetic participants showed mean serum glucagon levels increased with age ($p=0.007$). Non-Black participants had higher mean serum glucagon levels than Black participants ($p=0.024$) among the nondiabetics.

In its continuous form, α-1-C hemoglobin increased with age ($p<0.001$) and body fat ($p<0.001$). Black participants had higher α-1-C hemoglobin levels than the non-Black participants ($p<0.001$). Enlisted flyers had the highest mean α-1-C hemoglobin levels followed by the enlisted groundcrew and officers ($p=0.003$). Participants with a family history of diabetes had higher mean α-1-C hemoglobin levels than those participants without family history of diabetes ($p<0.001$). The analysis of diabetic participants revealed that mean α-1-C hemoglobin levels decreased as diabetic severity increased ($p<0.001$). Black diabetic participants had higher mean α-1-C hemoglobin levels than non-Black diabetic participants ($p=0.001$). Diabetic participants with a family history of diabetes had higher α-1-C hemoglobin levels than diabetic participants with no family history of diabetes ($p=0.025$). Analysis of nondiabetic participants showed mean α-1-C hemoglobin levels increased with age ($p<0.001$) and body fat ($p=0.001$). Nondiabetic enlisted flyers had the highest mean α-1-C hemoglobin levels followed by the nondiabetic enlisted groundcrew and nondiabetic officers ($p=0.001$). Black nondiabetic participants had higher mean α-1-C hemoglobin levels than non-Black nondiabetic participants ($p<0.001$). Nondiabetic participants with a family history of diabetes had higher α-1-C hemoglobin levels than nondiabetic participants with no family history of diabetes ($p=0.001$).

When categorized as normal or high, α-1-C hemoglobin revealed that the percentage of participants with high α-1-C hemoglobin levels increased with age ($p<0.001$) and decreased with body fat ($p<0.001$) for all participants. Enlisted flyers had the highest percentage of low α-1-C hemoglobin levels followed by enlisted groundcrew and officers ($p=0.001$). Black participants had a higher percentage of low α-1-C hemoglobin levels than non-Black participants ($p<0.001$). The participants with a family history of diabetes had a higher percentage of low α-1-C hemoglobin levels ($p<0.001$). The percentage of diabetic participants with low α-1-C hemoglobin levels decreased as body fat increased ($p=0.013$). All participants who treat their diabetes through diet only and those that do not treat their diabetes were in the low α-1-C hemoglobin category. Insulin dependent participants had a higher percentage of low α-1-C hemoglobin levels than participants using oral hypoglycemics ($p<0.001$).

Analysis of the nondiabetic cohort showed the percentage of participants with low α-1-C hemoglobin decreased with body fat ($p=0.004$). The low α-1-C hemoglobin category contained a greater percentage of enlisted flyers followed by enlisted groundcrew and officers ($p=0.004$). A higher percentage of nondiabetic participants were Black than were non-Black ($p<0.001$). A higher percentage of participants with low α-1-C hemoglobin had a family history of diabetes than those who had no history of diabetes ($p=0.024$).

The percentage of participants with positive results for urinary protein decreased as diabetic severity increased ($p=0.004$).

Serum proinsulin in its continuous form increased as body fat increased ($p<0.001$). Participants with Type B personalities had higher mean serum proinsulin levels than participants with Type A personalities ($p=0.021$). Non-Black participants had higher mean serum proinsulin levels than Black participants ($p=0.019$). Diabetic participants who treat their diabetes with insulin had the highest mean serum proinsulin level followed by

participants who treat their diabetes through diet only, participants not treating their diabetes, and participants who treat their diabetes with oral hypoglycemics ($p=0.004$).

Categorizing serum proinsulin as normal or abnormally high showed that abnormally high serum proinsulin levels decreased as body fat increased ($p=0.025$). Diabetic participants who treat their diabetes through diet only had the highest percent abnormal serum proinsulin levels followed by participants who do not treat their diabetes, participants who use oral hypoglycemics, and participants who are insulin dependent ($p<0.001$).

Serum C peptide in its continuous form increased with body fat ($p=0.001$) and diabetic severity ($p<0.001$). Black participants had lower mean serum C peptide levels than non-Black participants ($p=0.003$). Participants with a family history of diabetes had lower mean serum C peptide levels than participants with no family history of diabetes ($p=0.010$).

The percentage of participants with abnormal serum C peptide levels decreased as body fat increased ($p=0.068$). A lower percentage of participants with a family history of diabetes had abnormal serum C peptide levels than participants without a family history of diabetes ($p=0.072$). The percentage of participants with abnormal serum C peptide levels decreased as diabetic severity increased ($p<0.001$).

Total testosterone in its continuous form decreased with age ($p<0.001$) and body fat ($p<0.001$). Mean total testosterone levels were highest in the enlisted groundcrew followed by the enlisted flyers and officers ($p=0.014$). Total testosterone, when categorized as either low or normal, decreased as body fat increased ($p<0.001$).

Free testosterone in its continuous form decreased with age ($p<0.001$) and body fat ($p<0.001$). Mean free testosterone levels were highest among the enlisted groundcrew followed by the enlisted flyers and officers ($p<0.001$). Participants with Type A personalities had higher mean free testosterone levels than participants with Type B personalities ($p=0.001$).

Free testosterone, when categorized as either low or normal, decreased with age ($p<0.001$) and body fat ($p<0.001$). A higher percentage of participants with abnormally low free testosterone levels had Type B personalities rather than Type A personalities ($p=0.016$).

A higher percentage of Black participants had abnormally low sex hormone binding globulin than non-Black participants ($p=0.010$). A higher percentage of participants with abnormally low hormone binding globulin levels had Type B personalities rather than Type A personalities ($p=0.036$).

The ratio of total testosterone to sex hormone binding globulin increased with age ($p<0.001$).

Estradiol in its continuous form decreased with age ($p<0.001$). Black participants had higher mean estradiol levels than the non-Black participants ($p<0.001$).

Luteinizing hormone in both its continuous and discrete forms increased with age ($p<0.001$).

Follicle stimulating hormone in its continuous form increased with age ($p<0.001$). Mean follicle stimulating hormone levels were highest in the officers followed by the enlisted flyers and enlisted groundcrew ($p=0.005$).

Follicle stimulating hormone, when classified as normal or high, increased with age. The enlisted flyers had the highest percentage of abnormally high follicle stimulating hormone levels followed by the officers and enlisted groundcrew ($p=0.024$).

Exposure Analysis

The following section presents the results of the statistical analyses of the dependent variables shown in Table 18-1. Dependent variables are grouped into three sections: those derived and verified from a review of medical records, data obtained during the 1992 physical examination, and data derived from the laboratory portion of the 1992 followup examination.

Unadjusted and adjusted analyses of six models are presented for each variable. Model 1 examines the relationship between the dependent variable and group (Ranch Hand or Comparison). Model 2 explores the relationship between the dependent variable and an extrapolated initial dioxin measure for Ranch Hands who had a 1987 dioxin level greater than 10 ppt. If a participant did not have a 1987 dioxin level, a 1992 level was used. A statistical adjustment for the percent of body fat at the participant's time of duty in SEA and the change in the percent body fat from the participant's time of duty in SEA to the date of the blood draw for dioxin is included in this model to account for body-fat-related differences in elimination rate (42). Model 3 dichotomizes the Ranch Hands in Model 2 based on their initial dioxin measures; these two categories of Ranch Hands are referred to as the "low Ranch Hand" category and the "high Ranch Hand" category. These participants are added to Ranch Hands and Comparisons with current serum dioxin levels (1987, if available; 1992, if the 1987 level was not available) at or below 10 ppt to create a total of four categories. Ranch Hands with current serum dioxin levels at or below 10 ppt are referred to as the "background Ranch Hand" category. The relationship between the dependent variable in each of the three Ranch Hand categories and the dependent variable in the "Comparison" category is examined. A fourth contrast, exploring the relationship of the dependent variable in the low Ranch Hand category and the high Ranch Hand category combined, also is conducted. This combination is referred to in the text and tables as the "low plus high Ranch Hand" category. As in Model 2, a statistical adjustment is made for percent body fat at the participant's time of duty in SEA and the change in the percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

Models 4, 5, and 6 examine the relationship between the dependent variable and 1987 dioxin levels in all Ranch Hands with a dioxin measurement. If a participant did not have a 1987 dioxin measurement, a 1992 measurement was utilized in determining the current dioxin level. The measure of dioxin in Model 4 is lipid-adjusted, whereas whole-weight dioxin is used in Models 5 and 6. Model 6 differs from Model 5 in that a statistical adjustment for total lipids is included in Model 6. Further details on dioxin and the modeling strategy are found in Chapters 2 and 7 respectively.

Results of investigations for group-by-covariate and dioxin-by-covariate interactions are referenced in the text, and tabular results are presented in Appendix N-2. As described previously, additional analyses were performed when occupation, body fat, cholesterol, or HDL was retained in the final model for Models 2 through 6. Results excluding these covariates from these models are tabled in Appendix N-3, and dioxin-by-covariate interactions with these covariates excluded from these models are presented in Appendix N-4. Results from analyses excluding occupation, body fat, cholesterol, and HDL are discussed in the text only if a meaningful change in the results occurred (that is, changes between significant results, marginally significant results, and nonsignificant results).

Medical Records Variable

Past Thyroid Disease

The overall and stratified Model 1 unadjusted analyses of past thyroid disease did not show a significant difference between Ranch Hands and Comparisons (Table 18-3(a): $p>0.29$ for all analyses). In the adjusted analysis, the interaction of group and personality type was significant (Table 18-3(b): $p=0.039$). Appendix Table N-2-1 shows the stratified results of the relationship of past thyroid disease separately for Type A and Type B personalities. Removal of the interaction from the final model did not lead to a significant group effect ($p>0.19$ for all analyses). Age and the race-by-personality type interaction were significant.

Models 2 and 3 examined the relationship between past thyroid disease and initial dioxin. For Model 2, neither the unadjusted nor the adjusted analyses detected a significant initial dioxin effect (Table 18-3(c,d): $p>0.36$ for all analyses). Although the Model 3 unadjusted analysis showed nonsignificant results (Table 18-3(e): $p>0.26$ for all analyses), the adjusted analysis revealed a significant interaction between categorized dioxin and personality type (Table 18-3(f): $p=0.039$). Appendix Table N-2-1 displays further analysis of this interaction. The association between categorized dioxin and past thyroid disease was not significant, however, once the interaction was removed from the final model (Table 18-3(f): $p>0.19$). The interaction of age and race was retained in both Model 2 and 3 adjusted analyses. In addition, the race-by-personality type interaction was retained in the Model 3 analysis.

The Model 4 unadjusted analysis revealed no significant results, while in the adjusted analysis, the interaction of current dioxin and personality type was significant (Table 18-3(h): $p=0.037$). Results from additional analysis on this interaction are shown in Appendix Table N-2-1. Current dioxin was not significant once the interaction was removed from the final model ($p=0.954$). The association between current dioxin and past thyroid disease was nonsignificant in the unadjusted and adjusted analyses of Models 5 and 6 (Table 18-3(g,h): $p>0.54$ for all analyses). The age-by-race interaction was retained in each of the three adjusted analyses. Personality type was retained in the Model 5 and 6 analyses.

Table 18-3.
Analysis of Past Thyroid Disease

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	Group	n	Percent Yes	Est. Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*945*	*5.3*	*0.93 (0.64,1.35)*	*0.787*
	Comparison	*1,275*	*5.6*		
Officer	Ranch Hand	364	6.3	1.09 (0.62,1.92)	0.869
	Comparison	499	5.8		
Enlisted Flyer	Ranch Hand	161	5.0	1.46 (0.52,4.13)	0.646
	Comparison	203	3.4		
Enlisted Groundcrew	Ranch Hand	420	4.5	0.71 (0.40,1.25)	0.291
	Comparison	573	6.3		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks[a]
All	*0.92 (0.63,1.33)***	*0.655***	GROUP*PERS (p=0.039) AGE (p=0.006) RACE*PERS (p=0.008)
Officer	1.08 (0.61,1.90)**	0.791**	
Enlisted Flyer	1.48 (0.52,4.18)**	0.463**	
Enlisted Groundcrew	0.68 (0.39,1.22)**	0.196**	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

** Group-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table N-2-1 for further analysis of this interaction.

Table 18-3. (Continued)
Analysis of Past Thyroid Disease

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	174	5.7	1.08 (0.80,1.47)	0.621
Medium	171	2.9		
High	171	5.3		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
516	1.17 (0.84,1.62)	0.365	AGE*RACE (p=0.037)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 18-3. (Continued)
Analysis of Past Thyroid Disease

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Percent Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,057	5.9		
Background RH	371	6.7	1.22 (0.75,1.98)	0.421
Low RH	258	4.3	0.71 (0.37,1.37)	0.305
High RH	258	5.0	0.81 (0.44,1.50)	0.500
Low plus High RH	516	4.7	0.76 (0.47,1.23)	0.267

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,056			DXCAT*PERS (p=0.039) AGE*RACE (p=0.050) RACE*PERS (p=0.012)
Background RH	371	1.17 (0.72,1.91)**	0.524**	
Low RH	257	0.64 (0.32,1.25)**	0.191**	
High RH	258	0.88 (0.47,1.64)**	0.678**	
Low plus High RH	515	0.75 (0.46,1.23)**	0.254**	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Categorized dioxin-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table N-2-1 for further analysis of this interaction.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.
DXCAT = Categorized Dioxin.

Table 18-3. (Continued)
Analysis of Past Thyroid Disease

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Yes/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	6.1 (294)	6.1 (297)	4.4 (296)	0.95 (0.78,1.17)	0.644
5	5.4 (298)	6.4 (296)	4.8 (293)	0.99 (0.83,1.17)	0.874
6[c]	5.4 (297)	6.4 (296)	4.8 (293)	0.94 (0.79,1.13)	0.543

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	886	0.99 (0.80,1.23)**	0.954**	CURR*PERS (p=0.037) AGE*RACE (p=0.028)
5	886	1.02 (0.85,1.22)	0.834	PERS (p=0.095) AGE*RACE (p=0.038)
6[d]	885	0.98 (0.81,1.19)	0.842	PERS (p=0.110) AGE*RACE (p=0.036)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table N-2-1 for further analysis of this interaction.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.
CURR = Log_2 (current dioxin + 1).

Medical Records and Laboratory Variables

Composite Diabetes Indicator

For Model 1, neither the unadjusted nor the adjusted analyses of composite diabetes indicator revealed a significant group effect (Table 18-4(a,b): p>0.15 for all analyses). Age, body fat, and the occupation-by-race and race-by-family history of diabetes interactions were significant in the adjusted analysis.

No significant relationship between initial dioxin and composite diabetes indicator was evident from the results of the Model 2 unadjusted analysis (Table 18-4(c): p=0.947). In the adjusted analysis, a significant initial dioxin-by-occupation interaction was found (Table 18-4(d): p=0.023). Appendix Table N-2-2 displays results stratified by occupation. After removing the initial dioxin-by-occupation interaction and adjusting for age, race, and family history of diabetes, a marginally significant interaction between initial dioxin and occupation was revealed (Table 18-4(d): p=0.075, Adj. RR=1.21).

The Model 3 unadjusted analysis did not detect a significant dioxin effect (Table 18-4(e): p>0.16). In the adjusted analysis, the interaction of categorized dioxin and occupation was significant. The results stratified by occupation interaction are displayed in Appendix Table N-2-2. Deleting this interaction from the final model did not reveal significant differences between any of the Ranch Hand categories and the Comparison group (Table 18-4(f): p>0.17 for all contrasts). However, the removal of occupation from the final model led to a marginally significant difference between the high Ranch Hand category and the Comparison group (Table N-3-1: p=0.091, Adj. RR=1.41). Age, race, and family history of diabetes were significant covariates.

Each of the Model 4, 5, and 6 unadjusted analyses revealed significant positive associations between current dioxin and the composite diabetes indicator (Table 18-4(g): p=0.005, Est. RR=1.19 for Model 4; p<0.001, Est. RR=1.20 for Model 5; and p=0.050, Est. RR=1.12 for Model 6). Likewise, the adjusted analyses for Models 4 through 6 revealed significant positive associations with current dioxin (Table 18-4(h): p=0.002, Adj. RR=1.26 for Model 4; p<0.001, Adj. RR=1.27 for Model 5; and p=0.041, Adj. RR=1.16 for Model 6). Age, race, body fat, and family history of diabetes were significant covariates in each of the three adjusted analyses. In addition, personality type was a significant covariate in the Model 6 adjusted analysis.

Diabetic Severity

In the unadjusted analysis of diabetic severity, the overall difference between Ranch Hands and Comparisons was marginally significant for the insulin dependent versus normal contrast (Table 18-5(a): p=0.084, Est. RR=1.93). Of the Ranch Hands, 1.8 percent were insulin dependent in contrast to 0.9 percent for Comparisons. After stratifying the analyses by occupation, the contrast was again marginally significant for the officer category where 2.7 percent of the Ranch Hands were insulin dependent compared to only 1.0 percent of the Comparisons (p=0.057, Est. RR=2.86). The group contrast for diet only versus nondiabetics was also marginally significant for officers (p=0.098, Est. RR=2.07). Relative risks for the

Table 18-4.
Analysis of Composite Diabetes Indicator

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Percent Diabetic	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***949***	***15.0***	***1.08 (0.85,1.37)***	***0.576***
	Comparison	***1,276***	***14.0***		
Officer	Ranch Hand	365	15.1	1.36 (0.91,2.02)	0.157
	Comparison	502	11.6		
Enlisted Flyer	Ranch Hand	162	15.4	0.84 (0.48,1.47)	0.642
	Comparison	202	17.8		
Enlisted Groundcrew	Ranch Hand	422	14.7	0.99 (0.69,1.41)	0.999
	Comparison	572	14.9		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks[a]
All	***1.09 (0.84,1.41)***	***0.504***	AGE (p<0.001) BFAT (p<0.001) OCC*RACE (p=0.003) RACE*FAMDIAB (p=0.039)
Officer	1.30 (0.85,1.97)	0.223	
Enlisted Flyer	0.86 (0.47,1.59)	0.630	
Enlisted Groundcrew	1.04 (0.71,1.53)	0.849	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 18-4. (Continued)
Analysis of Composite Diabetes Indicator

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Diabetic	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	173	17.9	1.01 (0.85,1.19)	0.947
Medium	172	18.0		
High	173	19.7		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)[c]		
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
506	1.21 (0.98,1.50)**	0.075**	INIT*OCC ($p=0.023$) AGE ($p<0.001$) RACE ($p=0.111$) FAMDIAB ($p=0.016$)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Log_2 (initial dioxin)-by-covariate interaction ($0.01<p\leq0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table N-2-2 for further analysis of this interaction.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.
INIT = Log_2 (initial dioxin).

Table 18-4. (Continued)
Analysis of Composite Diabetes Indicator

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Diabetic	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,059	14.0		
Background RH	373	11.3	1.00 (0.69,1.47)	0.988
Low RH	258	19.0	1.30 (0.90,1.89)	0.165
High RH	260	18.1	1.13 (0.77,1.65)	0.523
Low plus High RH	518	18.5	1.21 (0.90,1.63)	0.197

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,044			DXCAT*OCC (p=0.031) AGE (p<0.001) RACE (p=0.062) FAMDIAB (p<0.001)
Background RH	367	0.94 (0.63,1.41)**	0.774**	
Low RH	252	1.21 (0.82,1.79)**	0.340**	
High RH	254	1.27 (0.85,1.92)**	0.243**	
Low plus High RH	506	1.24 (0.91,1.69)**	0.174**	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Categorized dioxin-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table N-2-2 for further analysis of this interaction.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 18-4. (Continued)
Analysis of Composite Diabetes Indicator

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Diabetic/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	9.5 (294)	18.7 (299)	18.1 (298)	1.19 (1.05,1.34)	0.005
5	8.7 (299)	18.2 (296)	19.6 (296)	1.20 (1.08,1.34)	<0.001
6[c]	8.7 (298)	18.2 (296)	19.6 (296)	1.12 (1.00,1.26)	0.050

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	873	1.26 (1.09,1.46)	0.002	AGE (p<0.001) RACE (p=0.069) BFAT (p<0.001) FAMDIAB (p=0.004)
5	873	1.27 (1.11,1.45)	<0.001	AGE (p<0.001) RACE (p=0.059) BFAT (p<0.001) FAMDIAB (p=0.005)
6[d]	871	1.16 (1.01,1.34)	0.041	AGE (p<0.001) RACE (p=0.028) PERS (p=0.147) BFAT (p<0.001) FAMDIAB (p=0.005)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 18-5.
Analysis of Diabetic Severity

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED										
			Percent							
Occupational Category	Group	n	Non-Diabetic	No Treatment	Diet Only	Oral Hypoglycemic	Insulin Dependent	Contrast vs. Nondiabetic	Est. Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*950*	*85.1*	*8.2*	*3.2*	*1.8*	*1.8*	*No Treatment*	*0.96 (0.71,1.30)*	*0.770*
	Comparison	*1,278*	*86.0*	*8.7*	*2.5*	*1.9*	*0.9*	*Diet Only*	*1.28 (0.77,2.11)*	*0.346*
								Oral Hypoglycemic	*0.96 (0.51,1.80)*	*0.907*
								Insulin Dependent	*1.93 (0.91,4.06)*	*0.084*
Officer	Ranch Hand	365	84.9	8.0	3.6	0.8	2.7	No Treatment	1.30 (0.77,2.19)	0.329
	Comparison	502	88.5	6.4	1.8	2.4	1.0	Diet Only	2.07 (0.87,4.90)	0.098
								Oral Hypoglycemic	0.36 (0.10,1.28)	0.114
								Insulin Dependent	2.86 (0.97,8.46)	0.057
Enlisted Flyer	Ranch Hand	162	84.6	8.0	2.5	3.1	1.9	No Treatment	0.66 (0.32,1.35)	0.254
	Comparison	203	82.3	11.8	3.5	1.0	1.5	Diet Only	0.70 (0.20,2.43)	0.570
								Oral Hypoglycemic	3.05 (0.58,16.13)	0.190
								Insulin Dependent	1.22 (0.24,6.14)	0.811
Enlisted Groundcrew	Ranch Hand	423	85.3	8.5	3.1	2.1	1.0	No Treatment	0.88 (0.57,1.38)	0.587
	Comparison	573	85.2	9.6	2.8	1.8	0.7	Diet Only	1.10 (0.52,2.31)	0.805
								Oral Hypoglycemic	1.22 (0.49,3.03)	0.674
								Insulin Dependent	1.35 (0.27,6.76)	0.714

Table 18-5. (Continued)
Analysis of Diabetic Severity

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED				
Occupational Category	**Contrast vs. Nondiabetic**	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***No Treatment***	***0.94 (0.68,1.29)***	***0.684***	AGE ($p<0.001$)
	Diet Only	***1.27 (0.76,2.13)***	***0.365***	OCC ($p=0.030$)
	Oral Hypoglycemic	***0.99 (0.52,1.88)***	***0.965***	FAMDIAB ($p<0.001$)
	Insulin Dependent	***1.82 (0.85,3.88)***	***0.124***	BFAT*RACE ($p=0.011$)
Officer	No Treatment	1.19 (0.69,2.06)	0.528	
	Diet Only	2.02 (0.85,4.84)	0.113	
	Oral Hypoglycemic	0.35 (0.09,1.26)	0.106	
	Insulin Dependent	2.77 (0.93,8.25)	0.067	
Enlisted Flyer	No Treatment	0.69 (0.33,1.45)	0.323	
	Diet Only	0.66 (0.19,2.36)	0.525	
	Oral Hypoglycemic	2.93 (0.53,16.05)	0.216	
	Insulin Dependent	0.86 (0.14,5.26)	0.869	
Enlisted Groundcrew	No Treatment	0.89 (0.56,1.42)	0.627	
	Diet Only	1.13 (0.53,2.43)	0.755	
	Oral Hypoglycemic	1.35 (0.53,3.44)	0.535	
	Insulin Dependent	1.39 (0.34,5.65)	0.647	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 18-5. (Continued)
Analysis of Diabetic Severity

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED

Initial Dioxin Category	n	Initial Dioxin Category Summary Statistics — Percent: Non-Diabetic	No Treatment	Diet Only	Oral Hypoglycemic	Insulin Dependent	Analysis Results for Log_2 (Initial Dioxin)[a]: Contrast vs. Nondiabetic	Est. Relative Risk (95% C.I.)[b]	p-Value
Low	173	82.1	9.8	4.6	2.3	1.2	No Treatment	0.88 (0.70,1.12)	0.311
Medium	172	82.0	9.9	2.9	1.7	3.5	Diet Only	1.00 (0.73,1.39)	0.979
High	173	80.4	8.1	5.2	5.8	0.6	Oral Hypoglycemic	1.44 (1.03,2.00)	0.032
							Insulin Dependent	0.83 (0.50,1.38)	0.467

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED

n	Contrast vs. Nondiabetic	Analysis Results for Log_2 (Initial Dioxin)[c]: Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
506	No Treatment	1.00 (0.75,1.33)	0.982	AGE (p<0.001) FAMDIAB*OCC (p=0.007) BFAT*RACE (p=0.006)
	Diet Only	1.29 (0.86,1.95)	0.224	
	Oral Hypoglycemic	2.37 (1.42,3.96)	0.001	
	Insulin Dependent	1.24 (0.60,2.57)	0.566	

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 18-5. (Continued)
Analysis of Diabetic Severity

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED						
		Percent				
Dioxin Category	n	Nondiabetic	No Treatment	Diet Only	Oral Hypoglycemic	Insulin Dependent
Comparison	1,060	86.0	8.1	2.8	1.9	1.1
Background RH	374	88.8	7.0	2.1	0.0	2.1
Low RH	258	81.0	10.9	4.3	1.9	1.9
High RH	260	81.9	7.7	4.2	4.6	1.5
Low plus High RH	518	81.5	9.3	4.3	3.3	1.7

	Contrast vs. Nondiabetic							
	No Treatment		Diet Only		Oral Hypoglycemic		Insulin Dependent	
Dioxin Category	Est. Relative Risk (95% C.I.)[ab]	p-Value	Est. Relative Risk (95% C.I.)[ab]	p-Value	Est. Relative Risk (95% C.I.)[ab]	p-Value	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison								
Background RH	1.04 (0.65,1.66)	0.863	0.92 (0.42,2.05)	0.845	--	--	2.24 (0.89,5.61)	0.086
Low RH	1.30 (0.82,2.07)	0.270	1.46 (0.72,2.99)	0.298	0.92 (0.33,2.53)	0.870	1.51 (0.52,4.39)	0.447
High RH	0.85 (0.51,1.43)	0.545	1.34 (0.65,2.74)	0.430	1.94 (0.91,4.16)	0.088	1.11 (0.34,3.61)	0.862
Low plus High RH	1.07 (0.73,1.56)	0.740	1.40 (0.79,2.47)	0.251	1.46 (0.74,2.87)	0.275	1.31 (0.54,3.20)	0.555

Table 18-5. (Continued)
Analysis of Diabetic Severity

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED					
		No Treatment vs. Nondiabetic		Diet Only vs. Nondiabetic	
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Adj. Relative Risk (95% C.I.)[ac]	p-Value
Comparison	1,045				
Background RH	368	0.87 (0.53,1.42)	0.569	0.86 (0.38,1.92)	0.708
Low RH	252	1.15 (0.71,1.86)	0.567	1.33 (0.64,2.79)	0.447
High RH	254	1.08 (0.63,1.84)	0.778	1.66 (0.79,3.48)	0.178
Low plus High RH	506	1.12 (0.76,1.66)	0.567	1.48 (0.83,2.66)	0.187

		Oral Hypoglycemic vs. Nondiabetic		Insulin Dependent vs. Nondiabetic		
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,045					AGE ($p<0.001$) FAMDIAB ($p<0.001$) BFAT*RACE ($p=0.001$)
Background RH	368	--	--	2.07 (0.82,5.27)	0.126	
Low RH	252	0.75 (0.26,2.15)	0.594	1.33 (0.45,3.95)	0.604	
High RH	254	2.44 (1.07,5.57)	0.033	1.11 (0.30,4.16)	0.879	
Low plus High RH	506	1.45 (0.71,2.96)	0.304	1.24 (0.49,3.16)	0.649	

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of duty in SEA and change in body fat from the time of duty in SEA to the date of the blood draw for dioxin.
[c] Adjusted for percent body fat at the time of duty in SEA, change in body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

--: Adjusted relative risk, confidence interval, and p-value not presented due to the sparse number of abnormalities.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 18-5. (Continued)
Analysis of Diabetic Severity

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED											
	Current Dioxin Category Summary Statistics							Analysis Results for Log_2 (Current Dioxin + 1)		
			Percent							
Model[a]	Current Dioxin Category	n	Non-Diabetic	No Treatment	Diet Only	Oral Hypoglycemic	Insulin Dependent	Contrast vs. Nondiabetic	Est. Relative Risk (95% C.I.)[b]	p-Value
4	Low	295	90.5	5.8	1.4	0.0	2.4	No Treatment	1.10 (0.93,1.29)	0.266
	Medium	299	81.3	10.7	5.0	1.3	1.7	Diet Only	1.27 (1.00,1.62)	0.052
	High	298	81.9	8.4	3.7	4.4	1.7	Oral Hypoglycemic	2.17 (1.59,2.96)	<0.001
								Insulin Dependent	0.75 (0.52,1.08)	0.120
5	Low	300	91.3	5.3	1.0	0.0	2.3	No Treatment	1.11 (0.97,1.29)	0.140
	Medium	296	81.8	10.8	4.7	1.4	1.4	Diet Only	1.35 (1.08,1.68)	0.007
	High	296	80.4	8.8	4.4	4.4	2.0	Oral Hypoglycemic	2.12 (1.57,2.85)	<0.001
								Insulin Dependent	0.80 (0.61,1.05)	0.114
6[c]	Low	299	91.3	5.4	1.0	0.0	2.3	No Treatment	1.12 (0.96,1.30)	0.155
	Medium	296	81.8	10.8	4.7	1.4	1.4	Diet Only	1.30 (1.04,1.63)	0.020
	High	296	80.4	8.8	4.4	4.4	2.0	Oral Hypoglycemic	2.16 (1.59,2.93)	<0.001
								Insulin Dependent	0.78 (0.59,1.03)	0.075

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 18-5. (Continued)
Analysis of Diabetic Severity

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED					
			Analysis Results for Log_2 (Current Dioxin)		
Model[a]	n	Contrast	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	874	No Treatment	1.04 (0.83,1.30)**	0.718**	CURR*OCC ($p=0.046$)
		Diet Only	1.61 (1.14,2.28)**	0.007**	AGE ($p<0.001$)
		Oral Hypoglycemic	3.96 (2.17,7.21)**	<0.001**	BFAT*RACE ($p=0.008$)
		Insulin Dependent	0.71 (0.43,1.17)**	0.177**	FAMDIAB*BFAT ($p=0.006$)
5	874	No Treatment	1.08 (0.89,1.31)**	0.453**	CURR*OCC ($p=0.028$)
		Diet Only	1.77 (1.29,2.44)**	<0.001**	AGE ($p<0.001$)
		Oral Hypoglycemic	3.90 (2.20,6.89)**	<0.001**	FAMDIAB*BFAT ($p=0.010$)
		Insulin Dependent	0.78 (0.55,1.11)**	0.168**	BFAT*RACE ($p=0.005$)
6[c]	873	No Treatment	****	****	CURR*AGE ($p<0.001$)
		Diet Only	****	****	FAMDIAB ($p=0.027$)
		Oral Hypoglycemic	****	****	BFAT ($p<0.001$)
		Insulin Dependent	****	****	

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interaction ($0.01<p\leq0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table N-2-3 for further analysis of this interaction.

**** Log_2 (current dioxin + 1)-by-covariate interaction ($p\leq0.01$); adjusted relative risk, confidence interval, and p-value not presented; refer to Appendix Table N-2-3 for further analysis of this interaction.

enlisted flyer and groundcrew categories were nonsignificant ($p>0.19$). After adjusting for age, occupation, family history of diabetes, and the body fat-by-race interaction, a marginally significant positive difference between Ranch Hands and Comparisons remained in the officer stratum for the insulin dependent category (Table 18-5(b): $p=0.067$, Adj. RR=2.77). All other adjusted results were nonsignificant ($p>0.11$).

The association between initial dioxin and diabetic severity was significant for the oral hypoglycemic category in the unadjusted Model 2 analysis (Table 18-5(c): $p=0.032$, Est. RR=1.44). Frequencies showed that for the low, medium, and high categories of initial dioxin, 2.3 percent, 1.7 percent, and 5.8 percent of Ranch Hands treated their diabetes with oral hypoglycemics. Adjusting for covariate information showed similar results. Significant covariates in Model 2 were age and the occupation-by-family history of diabetes and body fat-by-race interactions. Diabetic severity was significantly associated with initial dioxin for the oral hypoglycemic category (Table 18-5(d): $p=0.001$, Adj. RR=2.37). The Model 3 unadjusted analysis revealed a marginally significant positive difference between high Ranch Hands and Comparisons for the oral hypoglycemic category of diabetic severity (Table 18-5(e): $p=0.088$, Est. RR=1.94). For high Ranch Hands, 4.6 percent used oral hypoglycemics compared to only 1.9 percent of the Comparisons. Also, a greater percentage of background Ranch Hands were insulin dependent (2.1 %) in contrast to the Comparisons (1.1 %) ($p=0.086$, Est. RR=2.24). After adjusting for age, family history of diabetes, and the body fat-by-race interaction, the difference between high Ranch Hands and Comparisons remained significant for the oral hypoglycemic category (Table 18-5(f): $p=0.033$, Adj. RR=2.44), although the contrast between background Ranch Hands and Comparisons in the insulin dependent category became nonsignificant ($p=0.126$).

In the Models 4 and 5 unadjusted analyses, a significant positive association with current dioxin was disclosed for the diet only category of diabetic severity (Table 18-5(g): $p=0.052$, Est. RR=1.27 for Model 4 and $p=0.007$, Est. RR=1.35) for Model 5. For the low, medium, and high categories of current lipid-adjusted dioxin, 1.4, 5.0, and 3.7 percent of Ranch Hands used diet alone to treat their diabetes. For the current whole-weight dioxin categories, these percentages were 1.0, 4.7, and 4.4 respectively. Also, in each of the Model 4 through Model 6 unadjusted analyses, diabetic severity exhibited a highly positive significant association with current dioxin for the oral hypoglycemic category ($p<0.001$, Est. RR=2.17 for Model 4; $p<0.001$, Est. RR=2.12 for Model 5; $p<0.001$, Est. RR=2.06 for Model 6). The percentages of Ranch Hands using oral hypoglycemics in the low, medium, and high current lipid-adjusted dioxin categories were 0.0, 1.3, and 4.4. For Models 5 and 6, these percentages were 0.0, 1.4, and 4.4. Each of the adjusted analyses for Models 4, 5, and 6 revealed significant interactions with current dioxin. For Models 4 and 5, the interaction involved occupation (Table 18-5(h): $p=0.046$ for Model 4, $p=0.028$ for Model 5) whereas for Model 6 the interaction involved age ($p<0.001$). Appendix Table N-2-3 presents further analyses of these interactions. Highly significant positive results were evident for Models 4 and 5 after removing the interactions from the final models (supplemental analysis for Model 6 was not performed due to the significance level of the interaction term). The diet only and oral hypoglycemic categories of diabetic severity were each significantly associated with current dioxin for Models 4 and 5 (Model 4: $p=0.007$, Adj. RR=1.61 for normal vs. diet only and $p<0.001$, Adj. RR=3.96 for normal vs. oral hypoglycemic; Model 5: $p<0.001$, Adj. RR=1.77 for normal vs. diet only and $p<0.001$, Adj. RR=3.90 for normal vs. oral hypoglycemic).

Additional covariates significant for Models 4 and 5 were age and the body fat-by-race and body fat-by-family history of diabetes interactions. For Model 6, covariates retained were body fat and family history of diabetes.

Time to Diabetes Onset

The time to diabetes onset from time of duty in SEA did not differ significantly between Ranch Hands and Comparisons in the Model 1 unadjusted and adjusted analyses (Table 18-6(a,b): p>0.16 for all analyses). The significant covariates retained in the adjusted analysis were age, race, occupation, body fat, and family history of diabetes.

The association between time to diabetes onset and initial dioxin was not significant in the Model 2 analyses (Table 18-6(c,d): p>0.29 for the unadjusted and adjusted analyses). The adjusted analysis retained age, race, body fat, and family history of diabetes as significant covariates. In Model 3, the relationship between time to diabetes onset and categorized dioxin also was nonsignificant (Table 18-6(e,f): p>0.24 for all contrasts). Age, race, and family history of diabetes were retained in the adjusted analysis.

A significant negative association between time to diabetes onset and current dioxin was shown in Models 4, 5, and 6 (Table 18-6(g): p=0.004 for Model 4, p=0.001 for Model 5, and p=0.026 for Model 6). The time to diabetes onset from time of duty in SEA decreased with an increase in current serum dioxin levels. That is, Ranch Hands with high current serum dioxin levels tended to develop diabetes sooner after time of duty in SEA than Ranch Hands with lower serum dioxin levels. After adjusting for age, race, body fat, and family history of diabetes, the inverse association remained significant for Models 4, 5, and 6 (Table 18-6(h): p=0.001, p<0.001, and p=0.012 respectively).

Physical Examination Variables

Thyroid Gland

Less than one percent of the participants analyzed in the Model 1 and Models 3-6 analyses were found to have an abnormal thyroid gland at the physical examination; consequently, these models employed main effects only and interactions between candidate covariates were not considered. For Model 2, only one Ranch Hand with a lipid-adjusted initial dioxin level greater than 10 ppt (241.5 ppt) was found to have an abnormal thyroid gland; consequently, unadjusted and adjusted analyses were not performed.

Significant differences between Ranch Hands and Comparisons were not evident from the results of the Model 1 unadjusted analysis of thyroid gland (Table 18-7(a): p>0.62 for all analyses). No significant covariates were retained in the adjusted analysis; therefore, the results from this analysis were identical to those of the unadjusted analysis.

In the Model 3 unadjusted analysis of thyroid gland, no significant differences were revealed between the background, high, and low plus high Ranch Hand categories and the Comparison group (Table 18-7(e): p>0.16 for all analyses). In the low Ranch Hand category, there were no participants with an abnormal thyroid gland. The results of the

Table 18-6.
Analysis of Time to Diabetes Onset (years)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED				
Occupational Category	**Group**	**n**	**Coefficient (Std. Error)[a]**	**p-Value[b]**
All	***Ranch Hand***	***950***	***-0.0050 (0.0482)***	***0.917***
	Comparison	***1,277***		
Officer	Ranch Hand	365	-0.0836 (0.0759)	0.271
	Comparison	502		
Enlisted Flyer	Ranch Hand	162	0.1095 (0.1107)	0.323
	Comparison	203		
Enlisted Groundcrew	Ranch Hand	423	0.0192 (0.0755)	0.800
	Comparison	572		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED					
Occupational Category	**Group**	**n**	**Adj. Coefficient (Std. Error)[a]**	**p-Value[b]**	**Covariate Remarks[c]**
All	***Ranch Hand***	***932***	***0.0041***	***0.935***	AGE (p<0.001)
	Comparison	***1,259***	***(0.0499)***		RACE (p=0.051)
					OCC (p=0.011)
Officer	Ranch Hand	359	-0.0664	0.400	BFAT (p<0.001)
	Comparison	499	(0.0790)		FAMDIAB (p<0.001)
Enlisted Flyer	Ranch Hand	159	0.1638	0.161	
	Comparison	198	(0.1169)		
Enlisted Groundcrew	Ranch Hand	414	0.0046	0.953	
	Comparison	562	(0.0774)		

[a] Coefficient and standard error for group in a failure time analysis model, using a censored Weibull distribution. A negative coefficient implies that the time to diabetes onset is shorter for Ranch Hands than for Comparisons.

[b] P-value based on the group coefficient in a failure time analysis model, using a censored Weibull distribution.

[c] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 18-6. (Continued)
Analysis of Time to Diabetes Onset (years)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED			
Initial Dioxin Category Summary Statistics		Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Slope (Std. Error)[b]	p-Value
Low	173	0.0017 (0.0309)	0.957
Medium	172		
High	173		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED				
Initial Dioxin Category Summary Statistics		Analysis Results for Log_2 (Initial Dioxin)[c]		
Initial Dioxin	n	Adj. Slope (Std. Error)[b]	p-Value	Covariate Remarks
Low	171	-0.0344 (0.0329)	0.295	AGE ($p<0.001$)
Medium	167			RACE ($p=0.092$) BFAT ($p=0.077$)
High	168			FAMDIAB ($p=0.029$)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Slope and standard error based on time to diabetes onset versus $\log_2$ (initial dioxin) in a failure time analysis model, using a censored Weibull distribution.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 18-6. (Continued)
Analysis of Time to Diabetes Onset (years)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Coefficient (Std. Error)[ab]	p-Value[c]
Comparison	1,059		
Background RH	374	0.0477 (0.0741)	0.520
Low RH	258	-0.0777 (0.0700)	0.267
High RH	260	-0.0119 (0.0711)	0.867
Low plus High RH	518	-0.0443 (0.0559)	0.428

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Coefficient (Std. Error)[ad]	p-Value[c]	Covariate Remarks
Comparison	1,044			AGE ($p<0.001$) RACE ($p=0.030$) FAMDIAB ($p<0.001$)
Background RH	368	0.0908 (0.0785)	0.247	
Low RH	252	-0.0554 (0.0725)	0.445	
High RH	254	-0.0791 (0.0744)	0.287	
Low plus High RH	506	-0.0667 (0.0580)	0.250	

[a] Coefficient and standard error for Ranch Hand versus Comparison contrast in a failure time analysis model, using a censored Weibull distribution. A negative coefficient implies that the time to diabetes onset is shorter for the Ranch Hand category than for Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] P-value based on the Ranch Hand versus Comparison contrast in a failure time analysis model, using a censored Weibull distribution.

[d] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 18-6. (Continued)
Analysis of Time to Diabetes Onset (years)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category			Analysis Results for Log_2 (Current Dioxin + 1)	
	Low	Medium	High		
Model[a]	n	n	n	Slope (Std. Error)[b]	p-Value
4	295	299	298	-0.0694 (0.0238)	0.004
5	300	296	296	-0.0734 (0.0216)	0.001
6[c]	299	296	296	-0.0506 (0.0228)	0.026

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED			
	Analysis Results for Log_2 (Current Dioxin + 1)		
Model[a]	Adj. Slope (Std. Error)[b]	p-Value	Covariate Remarks
4	-0.0889 (0.0277)	0.001	AGE ($p<0.001$) RACE ($p=0.064$) BFAT ($p<0.001$) FAMDIAB ($p=0.009$)
5	-0.0925 (0.0251)	<0.001	AGE ($p<0.001$) RACE ($p=0.053$) BFAT ($p<0.001$) FAMDIAB ($p=0.009$)
6[d]	-0.0663 (0.0263)	0.012	AGE ($p<0.001$) RACE ($p=0.024$) BFAT ($p<0.001$) FAMDIAB ($p=0.008$)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Slope and standard error based on time to diabetes onset versus log_2 (current dioxin + 1) in a failure time analysis model, using a censored Weibull distribution.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 18-7.
Analysis of Thyroid Gland

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Abnormal**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	*Ranch Hand*	*931*	*0.5*	*0.67 (0.23,1.95)*	*0.628*
	Comparison	*1,242*	*0.8*		
Officer	Ranch Hand	357	0.6	0.90 (0.15,5.41)	0.999
	Comparison	482	0.6		
Enlisted Flyer	Ranch Hand	157	0.0	--	--
	Comparison	198	1.0		
Enlisted Groundcrew	Ranch Hand	417	0.7	0.81 (0.19,3.40)	0.999
	Comparison	562	0.9		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks**
All	*0.67 (0.23,1.95)*	*0.628*	
Officer	0.90 (0.15,5.41)	0.999	
Enlisted Flyer	--	--	
Enlisted Groundcrew	0.81 (0.19,3.40)	0.999	

--: Relative risk, confidence interval, and p-value not presented due to the sparse number of abnormalities.

Table 18-7. (Continued)
Analysis of Thyroid Gland

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	170	0.0	--	--
Medium	171	0.0	--	--
High	168	0.6	--	--

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[a]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
--	--	--	

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

--: Sample size, relative risk, confidence interval, and p-value not presented due to the sparse number of abnormalities.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 18-7. (Continued)
Analysis of Thyroid Gland

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,030	0.9		
Background RH	365	1.1	1.23 (0.37,4.07)	0.740
Low RH	254	0.0	--	--
High RH	255	0.4	0.45 (0.06,3.61)	0.453
Low plus High RH	509	0.2	0.23 (0.03,1.81)	0.162

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ab]	p-Value	Covariate Remarks
Comparison	1,030			
Background RH	365	1.23 (0.37,4.07)	0.740	
Low RH	254	--	--	
High RH	255	0.45 (0.06,3.61)	0.453	
Low plus High RH	509	0.23 (0.03,1.81)	0.162	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

--: Relative risk, confidence interval, and p-value not presented due to the sparse number of abnormalities.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 18-7. (Continued)
Analysis of Thyroid Gland

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Abnormal/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	1.0 (290)	0.3 (291)	0.3 (293)	0.67 (0.34,1.30)	0.222
5	1.0 (295)	0.3 (289)	0.3 (290)	0.78 (0.48,1.26)	0.332
6[c]	1.0 (294)	0.3 (289)	0.3 (290)	0.72 (0.44,1.18)	0.219

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	873	0.69 (0.35,1.34)	0.258	PERS (p=0.108)
5	873	0.80 (0.49,1.29)	0.372	PERS (p=0.104)
6[d]	872	0.74 (0.44,1.23)	0.265	PERS (p=0.116)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Model 3 adjusted analysis of thyroid gland duplicated those of the unadjusted analysis because no covariates were retained.

The unadjusted and adjusted analyses of Models 4, 5, and 6 revealed negative but nonsignificant associations between thyroid gland abnormality and current dioxin (Table 18-7(g,h): p>0.21 for all analyses). Personality type was found to be significant in each of the three adjusted analyses.

Testicular Volume: Minimum

In the unadjusted and adjusted Model 1 analyses of minimum testicular volume, no significant differences were found to exist between Ranch Hands and Comparisons (Table 18-8(a,b): p>0.69 for all analyses). Significant covariates included age, race, and body fat.

Minimum testicular volume was not significantly associated with initial dioxin in the unadjusted Model 2 analysis (Table 18-8(c): p=0.551). However, in the adjusted analysis, the interaction of initial dioxin and occupation was significant (Table 18-8(d): p=0.028) and upon deleting this interaction from the final model, a marginally significant negative dioxin effect remained (p=0.080, Slope=-0.3887). The results from analyzing the dioxin levels separately for each occupation are displayed in Appendix Table N-2-4. The minimum volume of the testes decreased as current dioxin increased. In addition, initial dioxin was significant after removing occupation from the final model (Appendix Table N-3-4: p=0.041). No significant results were revealed in either the unadjusted or adjusted Model 3 analyses of minimum testicular volume (Table 18-8(e,f): p>0.42 for all analyses). Significant covariates included age and race for Model 2 and age and the race-by-body fat interaction for Model 3.

For Models 4, 5, and 6, the unadjusted analyses of minimum testicular volume led to nonsignificant results (Table 18-8(g): p>0.46 for all analyses). In the Model 4 adjusted analysis, a marginally significant negative association between current dioxin and minimum testicular volume was detected (Table 18-8(h): p=0.080, Slope=-0.2301). No significant association with current dioxin was shown in the Model 5 adjusted analysis (p=0.203), although further adjusting for total lipids led to a significant interaction between current dioxin and occupation in the adjusted analysis for Model 6 (p=0.034). Appendix Table N-2-4 presents the results from further investigation of current dioxin stratified by occupation. A negative relationship of marginal significance between minimum testicular volume and current dioxin was found upon removing the interaction from the final model (p=0.075, Slope= -0.2411). Age and race were significant in each of the three current dioxin adjusted analyses.

Testicular Volume: Total

The unadjusted and adjusted Model 1 analyses of total testicular volume revealed no significant group effect (Table 18-9(a,b); p>0.60 for all analyses). Significant covariates included age, race, and body fat.

In the Model 2 and 3 unadjusted analyses, total testicular volume was not significantly associated with dioxin (Table 18-9(c,e): p>0.52 for all analyses). The adjusted Model 2 analysis revealed a significant interaction between initial dioxin and occupation

Table 18-8.
Analysis of Testicular Volume: Minimum (cm^3)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Mean**	**Difference of Means (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***937***	***15.94***	***0.03(-0.43,0.50)***	***0.887***
	Comparison	***1,270***	***15.90***		
Officer	Ranch Hand	360	15.72	0.09 (-0.66,0.84)	0.814
	Comparison	497	15.63		
Enlisted Flyer	Ranch Hand	161	15.80	-0.09 (-1.23,1.05)	0.877
	Comparison	202	15.89		
Enlisted Groundcrew	Ranch Hand	416	16.17	0.03 (-0.65,0.71)	0.929
	Comparison	571	16.14		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED						
Occupational Category	**Group**	**n**	**Adj. Mean**	**Difference of Adj. Means (95% C.I.)**	**p-Value**	**Covariate Remarks**[a]
All	***Ranch Hand***	***937***	***15.07***	***0.07 (-0.39,0.52)***	0.769	AGE ($p<0.001$) RACE ($p<0.001$) BFAT ($p=0.135$)
	Comparison	***1,270***	***15.00***			
Officer	Ranch Hand	360	15.20	0.15 (-0.59,0.88)	0.694	
	Comparison	497	15.05			
Enlisted Flyer	Ranch Hand	161	15.18	-0.06 (-1.17,1.06)	0.923	
	Comparison	202	15.24			
Enlisted Groundcrew	Ranch Hand	416	14.95	0.04 (-0.64,0.73)	0.901	
	Comparison	571	14.91			

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 18-8. (Continued)
Analysis of Testicular Volume: Minimum (cm^3)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[a]		
Initial Dioxin	n	Mean	Adj. Mean[a]	R^2	Slope (Std. Error)	p-Value
Low	172	15.33	15.31	0.001	-0.1166 (0.1954)	0.551
Medium	170	16.74	16.74			
High	171	15.64	15.65			

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED						
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[b]			
Initial Dioxin	n	Adj. Mean[b]	R^2	Adj. Slope (Std. Error)	p-Value	Covariate Remarks
Low	172	14.61**	0.063	-0.3887 (0.2218)**	0.080**	INIT*OCC (p=0.028) AGE (p<0.001) RACE (p=0.004)
Medium	170	15.81**				
High	171	14.33**				

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Log_2 (initial dioxin)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted mean, adjusted slope, standard error, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table N-2-4 for further analysis of this interaction.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 18-8. (Continued)
Analysis of of Testicular Volume: Minimum (cm^3)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Mean	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)	p-Value
Comparison	1,057	15.90	15.90		
Background RH	368	15.90	15.91	0.01 (-0.64,0.66)	0.973
Low RH	256	15.85	15.86	-0.05 (-0.79,0.70)	0.901
High RH	257	15.95	15.93	0.02 (-0.72,0.77)	0.950
Low plus High RH	513	15.90	15.89	-0.01 (-0.59,0.57)	0.968

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Mean[b]	Difference of Adj. Mean vs. Comparisons (95% C.I.)	p-Value	Covariate Remarks
Comparison	1,057	15.11			AGE ($p<0.001$) RACE*BFAT ($p=0.042$)
Background RH	368	15.27	0.16 (-0.49,0.80)	0.634	
Low RH	256	15.24	0.13 (-0.61,0.87)	0.734	
High RH	257	14.81	-0.30 (-1.05,0.44)	0.423	
Low plus High RH	513	15.04	-0.09 (-0.66,0.48)	0.767	

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 18-8. (Continued)
Analysis of Testicular Volume: Minimum (cm^3)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED						
	Current Dioxin Category Mean/(n)			Analysis Results for Log_2 (Current Dioxin + 1)		
Model[a]	Low	Medium	High	R^2	Slope (Std. Error)	p-Value
4	16.01 (292)	15.67 (294)	16.02 (295)	<0.001	-0.0782 (0.1307)	0.550
5	15.71 (297)	15.91 (292)	16.07 (292)	<0.001	-0.0285 (0.1122)	0.799
6[b]	15.79 (296)	15.92 (292)	16.00 (292)	0.002	-0.0880 (0.1211)	0.467

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED							
	Current Dioxin Category Adjusted Mean/(n)			Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	Low	Medium	High	R^2	Adj. Slope (Std. Error)	p-Value	Covariate Remarks
4	15.08 (292)	14.90 (294)	14.65 (295)	0.040	-0.2301 (0.1312)	0.080	AGE (p<0.001) RACE (p=0.004)
5	14.74 (297)	15.10 (292)	14.70 (292)	0.039	-0.1428 (0.1121)	0.203	AGE (p<0.001) RACE (p=0.004)
6[c]	14.90** (296)	15.18** (292)	14.72** (292)	0.049	-0.2411 (0.1352)**	0.075**	CURR*OCC (p=0.034) AGE (p<0.001) RACE (p=0.004)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Adjusted for log_2 total lipids.

[c] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted mean, adjusted slope, standard error, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table N-2-4 for further analysis of this interaction.

Note: Model 4: Low = ≤8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 18-9.
Analysis of Testicular Volume: Total (cm^3)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	*Ranch Hand*	*937*	*33.90*	*-0.14 --*	*0.766*
	Comparison	*1,270*	*34.04*		
Officer	Ranch Hand	360	33.40	-0.36 --	0.639
	Comparison	497	33.76		
Enlisted Flyer	Ranch Hand	161	33.86	-0.59 --	0.611
	Comparison	202	34.45		
Enlisted Groundcrew	Ranch Hand	416	34.35	0.21 --	0.753
	Comparison	571	34.13		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Group	n	Adj. Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]	Covariate Remarks[d]
All	*Ranch Hand*	*937*	*32.08*	*-0.07 --*	0.872	AGE ($p<0.001$)
	Comparison	*1,270*	*32.15*			RACE ($p<0.001$)
Officer	Ranch Hand	360	32.23	-0.25 --	0.730	BFAT ($p=0.103$)
	Comparison	497	32.48			
Enlisted Flyer	Ranch Hand	161	32.52	-0.51 --	0.642	
	Comparison	202	33.04			
Enlisted Groundcrew	Ranch Hand	416	31.90	0.23 --	0.727	
	Comparison	571	31.67			

[a] Transformed from the square root scale.

[b] Difference of means after transformation to original scale; confidence interval on difference of means not given because analysis was performed on square root scale.

[c] P-values based on difference of means on square root scale.

[d] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 18-9. (Continued)
Analysis of Analysis of Testicular Volume: Total (cm^3)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	172	32.87	32.86	0.001	-0.0202 (0.0329)	0.540
Medium	170	35.01	35.02			
High	171	33.35	33.35			

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED						
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[d]			
Initial Dioxin	n	Adj. Mean[ad]	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
Low	172	32.28**	0.078	-0.0708 (0.0374)**	0.059**	INIT*OCC (p=0.024) RACE (p=0.004) AGE*OCC (p=0.041)
Medium	170	33.74**				
High	171	31.30**				

[a] Transformed from square root scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Slope and standard error based on square root of total testicular volume versus $\log_2$ (initial dioxin).

[d] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Log_2 (initial dioxin)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted mean, adjusted slope, standard error, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table N-2-5 for further analysis of this interaction.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 18-9. (Continued)
Analysis of Testicular Volume: Total (cm^3)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,057	34.08	34.08		
Background RH	368	33.93	33.96	-0.12 --	0.857
Low RH	256	33.73	33.74	-0.34 --	0.653
High RH	257	33.74	33.69	-0.39 --	0.601
Low plus High RH	513	33.73	33.72	-0.36 --	0.529

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Mean[ae]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]	Covariate Remarks
Comparison	1,057	32.45			AGE ($p<0.001$) RACE ($p=0.001$)
Background RH	368	32.60	0.15 --	0.818	
Low RH	256	32.50	0.05 --	0.945	
High RH	257	31.51	-0.94 --	0.194	
Low plus High RH	513	32.03	-0.42 --	0.427	

[a] Transformed from square root scale.

[b] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Difference of adjusted means after transformation to original scale; confidence interval on difference of adjusted means not given because analysis was performed on square root scale.

[d] P-value is based on difference of means on square root scale.

[e] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 18-9. (Continued)
Analysis of Testicular Volume: Total (cm^3)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[b]	Current Dioxin Category Mean[a]/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) R^2	Slope (Std. Error)[c]	p-Value
4	34.09 (292)	33.48 (294)	33.88 (295)	0.001	-0.0175 (0.0220)	0.426
5	33.61 (297)	33.86 (292)	33.99 (292)	<0.001	-0.0094 (0.0189)	0.618
6[d]	33.75 (296)	33.88 (292)	33.85 (292)	0.002	-0.0194 (0.0204)	0.341

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[b]	Current Dioxin Category Adjusted Mean[a]/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
4	32.34 (292)	32.04 (294)	31.28 (295)	0.041	-0.0432 (0.0221)	0.051	AGE (p<0.001) RACE (p=0.005)
5	31.79 (297)	32.35 (292)	31.38 (292)	0.039	-0.0288 (0.0189)	0.128	AGE (p<0.001) RACE (p=0.005)
6[e]	32.05 (296)	32.43 (292)	31.24 (292)	0.042	-0.0424 (0.0205)	0.039	AGE (p<0.001) RACE (p=0.007)

[a] Transformed from square root scale.

[b] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[c] Slope and standard error based on square root of total testicular volume versus log_2 (current dioxin + 1).

Adjusted for log_2 total lipids.

[e] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤46 ppq; Medium = >46-128 ppq; High = >128 ppq.

(Table 18-9(d): p=0.024). Appendix Table N-2-5 presents detailed results of this interaction. In removing this interaction from the final model, a marginally significant initial dioxin effect was revealed (Table 18-9(d): p=0.059, Slope=-0.0708). The total volume of the testes decreased as current dioxin increased. Also, a significant association with initial dioxin was seen after removing occupation from the final model (Appendix Table N-3-5: p=0.032). In the adjusted analysis of Model 3, significant associations between total testicular volume and categorized dioxin were not detected (Table 18-9(f): p>0.19 for all contrasts).

No significant relationship between total testicular volume and current dioxin was revealed in any of the Model 4, 5, and 6 unadjusted analyses (Table 18-9(g): p>0.34 for all analyses). The Model 4 adjusted analysis revealed a marginally significant negative association with current dioxin (Table 18-9(h): p=0.051, Slope=-0.0432). Although the results of the Model 5 adjusted analysis were nonsignificant (p=0.128), a significant negative association between total testicular volume and current dioxin was seen in the Model 6 adjusted analysis (p=0.039, Slope=-0.0424). Age and race were covariates retained in all three current dioxin adjusted analyses.

Retinopathy Results (Diabetics)

No significant results were revealed in the Model 1 unadjusted analysis of retinopathy restricted to diabetics (Table 18-10(a): p>0.47 for all analyses). The adjusted analysis revealed a significant interaction between group and personality type (Table 18-10(b): p=0.018). Results of this interaction stratified by personality type are shown in Appendix Table N-2-6. Subsequent analysis with the interaction deleted from the final model did not reveal significant differences between Ranch Hands and Comparisons (Table 18-10(b): p>0.62 for all contrasts). Covariates retained in the adjusted analysis included family history of diabetes, diabetic severity, and the personality type-by-body fat interaction.

The Model 2 unadjusted analysis of retinopathy in diabetics did not reveal a significant association with initial dioxin (Table 18-10(c): p=0.144). Only five Ranch Hands (one with low initial dioxin and four with high initial dioxin levels) had retinopathy. This sparse number precluded meaningful adjusted analyses. Therefore, the adjusted relative risk, confidence interval, and p-value are not presented.

For Model 3, unadjusted and adjusted analyses did not reveal any statistically significant associations between retinopathy and categorized dioxin in diabetics (Table 18-10(e,f): p>0.15 for all contrasts). Personality type, family history of diabetes, and diabetic severity were significant covariates.

In the Model 4 unadjusted analysis, a marginally significant positive association between retinopathy and current lipid-adjusted dioxin was detected (Table 18-10(g): p=0.076, Est. RR=1.51). The low and medium current dioxin categories contained 3.7 and 3.6 percent retinal abnormalities, whereas the high category contained 7.4 percent. After adjusting for personality type, body fat, family history of diabetes, and diabetic severity, the relationship between current dioxin and retinopathy remained marginally significant (Table 18-10(h): p=0.066, Adj. RR=1.64). The Model 5 unadjusted analysis showed a marginally significant positive association with current whole-weight dioxin (Table 18-10(g): p=0.088, Est.

Table 18-10.
Analysis of Retinopathy Results (Diabetics)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Abnormal**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***141***	***5.0***	***1.81 (0.56,5.82)***	***0.479***
	Comparison	***178***	***2.8***		
Officer	Ranch Hand	54	3.7	1.06 (0.14,7.79)	0.999
	Comparison	57	3.5		
Enlisted Flyer	Ranch Hand	25	12.0	--	--
	Comparison	36	0.0		
Enlisted Groundcrew	Ranch Hand	62	3.2	0.91 (0.15,5.62)	0.999
	Comparison	85	3.5		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***1.42 (0.35,5.79)*****	***0.623*****	GROUP*PERS (p=0.018) FAMDIAB (p=0.018) DIABSEV (p<0.001) PERS*BFAT (p=0.024)
Officer	0.72 (0.07,7.47)**	0.787**	
Enlisted Flyer	--	--	
Enlisted Groundcrew	0.67 (0.08,5.63)**	0.710**	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

** Group-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table N-2-6 for further analysis of this interaction.

--: Relative risk, confidence interval, and p-value not presented due to the sparse number of abnormalities.

Table 18-10. (Continued)
Analysis of Retinopathy Results (Diabetics)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	31	3.2	1.59 (0.88,2.88)	0.144
Medium	31	0.0		
High	34	11.8		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[a]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
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[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

--: Sample size, adjusted relative risk, confidence interval, and p-value not presented due to the sparse number of abnormalities.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 18-10. (Continued)
Analysis of Retinopathy Results (Diabetics)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	147	2.7		
Background RH	41	4.9	1.87 (0.32,11.09)	0.490
Low RH	49	2.0	0.65 (0.07,6.03)	0.702
High RH	47	8.5	2.92 (0.67,12.80)	0.155
Low plus High RH	96	5.2	1.68 (0.42,6.66)	0.460

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	146			PERS ($p=0.027$) FAMDIAB ($p=0.007$) DIABSEV ($p<0.001$)
Background RH	38	1.99 (0.25,15.93)	0.515	
Low RH	48	0.57 (0.05,6.79)	0.660	
High RH	46	2.66 (0.43,16.38)	0.292	
Low plus High RH	94	1.46 (0.28,7.74)	0.654	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 18-10. (Continued)
Analysis of Retinopathy Results (Diabetics)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Abnormal/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	3.7 (27)	3.6 (56)	7.4 (54)	1.51 (0.97,2.36)	0.076
5	4.0 (25)	1.9 (54)	8.6 (58)	1.43 (0.95,2.15)	0.088
6[c]	4.0 (25)	1.9 (54)	8.6 (58)	1.47 (0.93,2.31)	0.103

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	132	1.64 (0.93,2.88)	0.066	PERS (p=0.001) BFAT (p=0.098) FAMDIAB (p=0.010) DIABSEV (p<0.001)
5	132	1.53 (0.91,2.57)	0.079	PERS (p=0.001) BFAT (p=0.101) FAMDIAB (p=0.013) DIABSEV (p=0.001)
6[d]	132	1.62 (0.93,2.83)	0.067	PERS (p=0.001) BFAT (p=0.099) FAMDIAB (p=0.011) DIABSEV (p=0.001)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

RR=1.43). The tracheotomized levels of current dioxin revealed abnormality in 4.0 percent of the Ranch Hands in the low category, 1.9 percent in the medium category, and 8.6 percent in the high category. A marginally significant positive relationship between current dioxin and retinopathy remained in the Model 5 adjusted analysis (Table 18-10(h): p=0.079, Adj. RR=1.53). Although no significant results were obtained in the unadjusted analysis for Model 6 (Table 18-10(g): p=0.103), adjusting for covariates led to a positive association of marginal significance between retinopathy and current dioxin (Table 18-10(h): p=0.067, Adj. RR=1.62). Personality type, body fat, family history of diabetes, and diabetic severity were retained in both the Model 5 and 6 adjusted analyses. When body fat was removed from the adjusted analyses of Models 4, 5, and 6, the association between current dioxin and retinopathy became nonsignificant (Appendix Table N-3-6: p>0.18 for each model).

Neuropathy Results (Diabetics)

Although no significant overall difference between Ranch Hands and Comparisons was evident from the Model 1 unadjusted analysis of diabetics (Table 18-11(a): p=0.150), stratification across occupation revealed a marginally significant difference between the two groups in the enlisted groundcrew category (p=0.076, Est. RR=3.44), where 14.5 percent of the diabetic Ranch Hands and 4.7 percent of the diabetic Comparisons had neuropathy. After adjusting for age, race, occupation, and diabetic severity, the difference between the two groups in the enlisted groundcrew category remained marginally significant (Table 18-11(b): p=0.098, Adj. RR=3.38). The overall adjusted contrast and the contrasts involving officers and enlisted flyers were nonsignificant (p>0.42).

Unadjusted and adjusted Model 2 analyses of neuropathy in diabetics did not reveal a significant association with initial dioxin (Table 18-11(c,d): p>0.42 for both analyses). Diabetic severity was the only significant covariate in the adjusted model. In addition, although the percentage of high Ranch Hands with neuropathy was greater than that of the Comparisons (17.0% vs. 7.4%), no significant results were shown in the Model 3 unadjusted analysis (Table 18-11(e): p>0.11 for all contrasts). However, after adjusting for age, race, diabetic severity, and the personality type-by-body fat interaction, results became significant for diabetic Ranch Hands in the high category (Table 18-11(f): p=0.076, Adj. RR=3.23). When body fat was removed from the final model, the difference between the high Ranch Hand category and the Comparisons became nonsignificant (Table N-3-7(a): p=0.131).

None of the Model 4 through 6 analyses detected any significant associations between current dioxin and neuropathy in diabetics (Table 18-11(g,h): p>0.32 for all analyses). Covariates retained in each of the adjusted analyses included occupation and four covariate-by-covariate interactions: age-by-race, age-by-personality type, body fat-by-diabetic severity, and family history of diabetes-by-diabetic severity.

Radial Pulses (Doppler) (Diabetics)

The sparse number of diabetic participants with abnormal radial pulses (one Ranch Hand and two Comparisons) prevented meaningful adjusted analyses for Models 1 through 6. Consequently, relative risks, confidence intervals, and p-values are not presented. Unadjusted analyses were performed for all models except Model 2, where there was only one Ranch

Table 18-11.
Analysis of Neuropathy Results (Diabetics)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Abnormal**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***142***	***12.0***	***1.89 (0.87,4.11)***	***0.150***
	Comparison	***179***	***6.7***		
Officer	Ranch Hand	55	9.1	1.83 (0.42,8.07)	0.656
	Comparison	58	5.2		
Enlisted Flyer	Ranch Hand	25	12.0	0.85 (0.18,3.91)	0.999
	Comparison	36	13.9		
Enlisted Groundcrew	Ranch Hand	62	14.5	3.44 (1.01,11.74)	0.076
	Comparison	85	4.7		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks**[a]
All	***1.45 (0.58,3.59)***	***0.425***	AGE (p=0.001) RACE (p=0.146) OCC (p=0.057) DIABSEV (p<0.001)
Officer	1.02 (0.18,5.80)	0.984	
Enlisted Flyer	0.52 (0.09,3.14)	0.474	
Enlisted Groundcrew	3.38 (0.80,14.30)	0.098	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 18-11. (Continued)
Analysis of Neuropathy Results (Diabetics)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	31	3.2	1.20 (0.77,1.87)	0.421
Medium	31	12.9		
High	34	17.6		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
96	1.20 (0.72,1.99)	0.476	DIABSEV (p=0.002)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 18-11. (Continued)
Analysis of Neuropathy Results (Diabetics)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	148	7.4		
Background RH	42	14.3	2.26 (0.74,6.86)	0.151
Low RH	49	6.1	0.68 (0.18,2.61)	0.570
High RH	47	17.0	2.30 (0.82,6.47)	0.115
Low plus High RH	96	11.5	1.37 (0.55,3.42)	0.502

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	148			AGE (p=0.013) RACE (p=0.009) DIABSEV (p<0.001) PERS*BFAT (p=0.030)
Background RH	42	2.04 (0.49,8.50)	0.329	
Low RH	49	0.35 (0.07,1.81)	0.210	
High RH	47	3.23 (0.89,11.77)	0.076	
Low plus High RH	96	1.22 (0.41,3.64)	0.721	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 18-11. (Continued)
Analysis of Neuropathy Results (Diabetics)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Abnormal/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	17.9 (28)	3.6 (56)	18.5 (54)	1.14 (0.83,1.57)	0.424
5	19.2 (26)	5.6 (54)	15.5 (58)	1.09 (0.83,1.44)	0.535
6[c]	19.2 (26)	5.6 (54)	15.5 (58)	1.17 (0.85,1.61)	0.321

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	133	1.01 (0.65,1.56)	0.973	OCC (p=0.079) AGE*RACE (p=0.048) AGE*PERS (p=0.014) BFAT*DIABSEV (p=0.006) FAMDIAB*DIABSEV (p=0.010)
5	133	1.00 (0.70,1.43)	0.995	OCC (p=0.066) AGE*RACE (p=0.048) AGE*PERS (p=0.014) FAMDIAB*DIABSEV (p=0.010) BFAT*DIABSEV (p=0.006)
6[d]	133	1.13 (0.73,1.74)	0.572	OCC (p=0.129) AGE*RACE (p=0.043) AGE*PERS (p=0.016) FAMDIAB*DIABSEV (p=0.006) BFAT*DIABSEV (p=0.005)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Hand with abnormal radial pulses. The unadjusted Model 1 analysis did not show any significant differences between Ranch Hands and Comparisons (Table 18-12(a): p>0.84 for all contrasts). No significant differences were revealed between any of the Ranch Hand categories and the Comparison group in the Model 3 unadjusted analysis (Table 18-12(e): p>0.26 for all analyses). For Models 4 through 6, the unadjusted analyses did not show any significant associations between current dioxin and radial pulses (Table 18-12(g): p>0.27 for all analyses).

Femoral Pulses (Doppler) (Diabetics)

The Model 1 unadjusted analysis of femoral pulses on diabetics did not reveal overall or stratified differences between Ranch Hands and Comparisons (Table 18-13(a): p>0.48 for all analyses). Likewise, adjusting for diabetic severity and current cigarette smoking did not show a significant group effect in the adjusted analysis (Table 18-13(b): p>0.53 for all contrasts). Neither the unadjusted nor the adjusted analyses for Models 2 and 3 detected a significant association between femoral pulses and dioxin (Table 18-13(c-f): p>0.21 for all analyses). The Model 2 adjusted analysis retained diabetic severity only, whereas, in the Model 3 adjusted analysis, current cigarette smoking also was significant. For Models 4 through 6, the unadjusted and adjusted analyses of femoral pulses showed no significant association with current dioxin (Table 18-13(g,h): p>0.57 for all analyses). Diabetic severity was the only covariate retained in each adjusted analysis.

Popliteal Pulses (Doppler) (Diabetics)

No significant group differences were obtained in either the unadjusted or adjusted analyses of popliteal pulses restricted to diabetics (Table 18-14(a,b): p>0.11 for all analyses). Diabetic severity and current cigarette smoking were retained in the adjusted analysis. The relationship between initial or categorized dioxin and popliteal pulses was determined to be nonsignificant in the unadjusted and adjusted analyses for Models 2 and 3 (Table 18-14(c-f): p>0.13 for all analyses). Significant covariates retained in each of the adjusted analyses included current cigarette smoking and age. Diabetic severity was significant in the adjusted analysis for Model 2. Results of the Models 4, 5, and 6 unadjusted and adjusted analyses are presented in Table 18-14(g,h). No significant current dioxin effect was revealed in any of these analyses (p>0.64 for all analyses). In each of the adjusted analyses, diabetic severity was significant.

Dorsalis Pedis Pulses (Doppler) (Diabetics)

Overall and stratified contrasts for Ranch Hands versus Comparisons were not significant in the Model 1 analyses of dorsalis pedis pulses restricted to diabetics (Table 18-15(a,b): p>0.31 for all contrasts). Age, body fat, and lifetime alcohol history were significant in the adjusted analysis.

The relationship between dorsalis pedis pulses and initial dioxin in diabetics was not significant in either the unadjusted or adjusted Model 2 analyses (Table 18-15(c,d): p>0.35). Significant covariates included family history of diabetes, lifetime alcohol history, high density lipoprotein, and family history of heart disease.

Table 18-12.
Analysis of Radial Pulses (Doppler) (Diabetics)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Abnormal**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***142***	***1.4***	***2.54 (0.23,28.33)***	***0.840***
	Comparison	***179***	***0.6***		
Officer	Ranch Hand	55	1.8	1.06 (0.06,17.30)	0.999
	Comparison	58	1.7		
Enlisted Flyer	Ranch Hand	25	0.0	--	--
	Comparison	36	0.0		
Enlisted Groundcrew	Ranch Hand	62	1.6	--	--
	Comparison	85	0.0		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	--	--	
Officer	--	--	
Enlisted Flyer	--	--	
Enlisted Groundcrew	--	--	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

--: Relative risk, confidence interval, and p-value not presented due to the sparse number of abnormalities.

Table 18-12. (Continued)
Analysis of Radial Pulses (Doppler) (Diabetics)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Percent Abnormal	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	31	3.2	--	--
Medium	31	0.0		
High	34	0.0		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)			
n	Adj. Relative Risk (95% C.I.)[a]	p-Value	Covariate Remarks
--	--	--	

[a] Relative risk for a twofold increase in initial dioxin.

--: Sample size, relative risk, confidence interval, and p-value not presented due to the sparse number of abnormalities.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 18-12. (Continued)
Analysis of Radial Pulses (Doppler) (Diabetics)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	**n**	**Percent Abnormal**	**Est. Relative Risk (95% C.I.)[ab]**	**p-Value**
Comparison	148	0.7		
Background RH	42	2.4	5.19 (0.23,96.2)	0.267
Low RH	49	2.0	2.48 (0.14,44.0)	0.533
High RH	47	0.0	--	--
Low plus High RH	96	1.0	1.14 (0.06,20.91)	0.932

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	**n**	**Adj. Relative Risk (95% C.I.)[ab]**	**p-Value**	**Covariate Remarks**
Comparison	--			
Background RH	--	--	--	
Low RH	--	--	--	
High RH	--	--	--	
Low plus High RH	--	--	--	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

--: Sample size, relative risk, confidence interval, and p-value not presented due to the sparse number of abnormalities.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 18-12. (Continued)
Analysis of Radial Pulses (Doppler) (Diabetics)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Abnormal/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	3.6 (28)	1.8 (56)	0.0 (54)	0.58 (0.22,1.53)	0.271
5	3.8 (26)	1.9 (54)	0.0 (58)	0.71 (0.38,1.30)	0.307
6[c]	3.8 (26)	1.9 (54)	0.0 (58)	0.78 (0.37,1.61)	0.515

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	--	--	--	
5	--	--	--	
6	--	--	--	

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

--: Sample size, relative risk, confidence interval, and p-value not presented due to the sparse number of abnormalities.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 18-13.
Analysis of Femoral Pulses (Doppler) (Diabetics)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Percent Abnormal	Est. Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*142*	*4.2*	*1.93 (0.53,6.98)*	*0.486*
	Comparison	*179*	*2.2*		
Officer	Ranch Hand	55	7.3	--	--
	Comparison	58	0.0		
Enlisted Flyer	Ranch Hand	25	4.0	0.71 (0.06,8.26)	0.999
	Comparison	36	5.6		
Enlisted Groundcrew	Ranch Hand	62	1.6	0.68 (0.06,7.68)	0.999
	Comparison	85	2.4		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks[a]
All	*1.53 (0.40,5.91)*	*0.533*	DIABSEV (p=0.262) CSMOK (p=0.032)
Officer	--	--	
Enlisted Flyer	0.58 (0.04,7.72)	0.680	
Enlisted Groundcrew	0.70 (0.06,8.25)	0.775	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

--: Relative risk, confidence interval, and p-value not presented due to the sparse number of abnormalities.

Table 18-13. (Continued)
Analysis of Femoral Pulses (Doppler) (Diabetics)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	31	6.5	0.73 (0.34,1.55)	0.377
Medium	31	3.2		
High	34	2.9		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
96	0.73 (0.34,1.57)	0.399	DIABSEV (p=0.718)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 18-13. (Continued)
Analysis of Femoral Pulses (Doppler) (Diabetics)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	148	2.0		
Background RH	42	2.4	1.29 (0.12,13.36)	0.833
Low RH	49	6.1	2.77 (0.53,14.56)	0.228
High RH	47	2.1	0.82 (0.08,8.89)	0.872
Low plus High RH	96	4.2	1.80 (0.38,8.56)	0.458

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	148			DIABSEV (p=0.704) CSMOK (p=0.006)
Background RH	42	1.25 (0.11,13.91)	0.857	
Low RH	49	2.93 (0.53,16.20)	0.217	
High RH	47	0.45 (0.03,6.25)	0.554	
Low plus High RH	96	1.49 (0.30,7.41)	0.627	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 18-13. (Continued)
Analysis of Femoral Pulses (Doppler) (Diabetics)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[a]	Current Dioxin Category Percent Abnormal/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) Est. Relative Risk (95% C.I.)[b]	p-Value
4	3.6 (28)	5.4 (56)	1.9 (54)	0.90 (0.49,1.63)	0.715
5	3.8 (26)	3.7 (54)	3.4 (58)	0.98 (0.61,1.60)	0.950
6[c]	3.8 (26)	3.7 (54)	3.4 (58)	0.86 (0.50,1.50)	0.606

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[a]	Analysis Results for Log_2 (Current Dioxin + 1) n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	138	0.89 (0.51,1.55)	0.674	DIABSEV (p=0.424)
5	138	0.98 (0.63,1.51)	0.911	DIABSEV (p=0.437)
6[d]	138	0.87 (0.52,1.44)	0.579	DIABSEV (p=0.453)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 18-14.
Analysis of Popliteal Pulses (Doppler) (Diabetics)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Percent Abnormal	Est. Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*142*	*6.3*	*2.96 (0.89,9.82)*	*0.117*
	Comparison	*179*	*2.2*		
Officer	Ranch Hand	55	10.9	--	--
	Comparison	58	0.0		
Enlisted Flyer	Ranch Hand	25	4.0	0.71 (0.06,8.26)	0.999
	Comparison	36	5.6		
Enlisted Groundcrew	Ranch Hand	62	3.2	1.38 (0.19,10.10)	0.999
	Comparison	85	2.4		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks[a]
All	*2.28 (0.65,8.03)*	*0.189*	DIABSEV (p=0.153) CSMOK (p=0.015)
Officer	--	--	
Enlisted Flyer	0.47 (0.03,6.39)	0.572	
Enlisted Groundcrew	1.31 (0.17,10.31)	0.799	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

--: Relative risk, confidence interval, and p-value not presented due to the sparse number of abnormalities.

Table 18-14. (Continued)
Analysis of Popliteal Pulses (Doppler) (Diabetics)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	31	6.5	0.90 (0.52,1.56)	0.699
Medium	31	9.7		
High	34	5.9		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
96	0.89 (0.45,1.77)	0.732	AGE (p=0.125) DIABSEV (p=0.075) CSMOK (p=0.029)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 18-14. (Continued)
Analysis of Popliteal Pulses (Doppler) (Diabetics)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	148	2.7		
Background RH	42	2.4	0.86 (0.09,8.21)	0.897
Low RH	49	6.1	2.10 (0.45,9.88)	0.348
High RH	47	8.5	3.04 (0.70,13.15)	0.137
Low plus High RH	96	7.3	2.54 (0.71,9.12)	0.154

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	148			DIABSEV (p=0.177) AGE (p=0.023) CSMOK (p<0.001)
Background RH	42	0.45 (0.04,5.58)	0.530	
Low RH	49	1.50 (0.28,7.97)	0.632	
High RH	47	2.62 (0.53,12.91)	0.235	
Low plus High RH	96	1.99 (0.52,7.62)	0.317	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 18-14. (Continued)
Analysis of Popliteal Pulses (Doppler) (Diabetics)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Abnormal/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	3.6 (28)	5.4 (56)	7.4 (54)	1.02 (0.65,1.62)	0.920
5	3.8 (26)	3.7 (54)	8.6 (58)	1.09 (0.74,1.61)	0.647
6[c]	3.8 (26)	3.7 (54)	8.6 (58)	0.97 (0.62,1.51)	0.884

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	138	0.97 (0.65,1.45)	0.878	DIABSEV (p=0.019)
5	138	1.04 (0.74,1.45)	0.821	DIABSEV (p=0.021)
6[d]	138	0.93 (0.63,1.37)	0.712	DIABSEV (p=0.021)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 18-15.
Analysis of Dorsalis Pedis Pulses (Doppler) (Diabetics)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Percent Abnormal	Est. Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*142*	*16.9*	*1.45 (0.78,2.71)*	*0.312*
	Comparison	*179*	*12.3*		
Officer	Ranch Hand	55	18.2	1.62 (0.57,4.61)	0.519
	Comparison	58	12.1		
Enlisted Flyer	Ranch Hand	25	12.0	0.68 (0.15,3.03)	0.890
	Comparison	36	16.7		
Enlisted Groundcrew	Ranch Hand	62	17.7	1.82 (0.70,4.71)	0.315
	Comparison	85	10.6		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks[a]
All	*1.16 (0.59,2.30)*	*0.668*	AGE (p=0.011)
Officer	1.33 (0.44,4.07)	0.616	BFAT (p=0.051)
Enlisted Flyer	0.62 (0.13,2.92)	0.543	DIABSEV (p=0.219)
Enlisted Groundcrew	1.42 (0.49,4.07)	0.515	DRKYR (p=0.022)

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 18-15. (Continued)
Analysis of Dorsalis Pedis Pulses (Doppler) (Diabetics)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	31	9.7	1.19 (0.83,1.70)	0.351
Medium	31	19.4		
High	34	23.5		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
88	1.20 (0.76,1.89)	0.448	FAMDIAB (p=0.138) DIABSEV (p=0.159) DRKYR (p=0.113) HDL (p=0.083) HRTDIS (p=0.075)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 18-15. (Continued)
Analysis of Dorsalis Pedis Pulses (Doppler) (Diabetics)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	148	12.8		
Background RH	42	14.3	0.96 (0.34,2.70)	0.932
Low RH	49	10.2	0.65 (0.22,1.89)	0.425
High RH	47	25.5	2.36 (0.99,5.59)	0.052
Low plus High RH	96	17.7	1.32 (0.63,2.77)	0.461

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	145			AGE (p=0.042) DIABSEV (p=0.336) DRKYR (p=0.027)
Background RH	42	0.57 (0.17,1.89)	0.354	
Low RH	47	0.39 (0.11,1.34)	0.133	
High RH	46	2.73 (1.11,6.72)	0.029	
Low plus High RH	93	1.21 (0.56,2.62)	0.631	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 18-15. (Continued)
Analysis of Dorsalis Pedis Pulses (Doppler) (Diabetics)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Abnormal/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	17.9 (28)	8.9 (56)	24.1 (54)	1.10 (0.83,1.46)	0.522
5	19.2 (26)	7.4 (54)	24.1 (58)	1.07 (0.84,1.36)	0.605
6[c]	19.2 (26)	7.4 (54)	24.1 (58)	1.04 (0.78,1.37)	0.807

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	133	1.33 (0.90,1.74)	0.183	DIABSEV (p=0.011) DRKYR (p=0.016)
5	133	****	****	CURR*PACKYR (p=0.007) DIABSEV (p=0.044) DRKYR (p=0.107) HRTDIS (p=0.064) CHOL (p=0.127)
6[d]	133	****	****	CURR*PACKYR (p=0.008) DIABSEV (p=0.065) DRKYR (p=0.101) HRTDIS (p=0.066) CHOL (p=0.115)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

**** Log_2 (current dioxin + 1)-by-covariate interaction ($p \leq 0.01$); adjusted relative risk, confidence interval, and p-value not presented; refer to Appendix Table N-2-7 for further analysis of this interaction.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

For Model 3, the percentage of diabetic Ranch Hands in the high category with abnormal dorsalis pedis pulses was significantly greater than that of the Comparisons (Table 18-15(e): 25.5% vs. 12.8%, p=0.052, Est. RR=2.36). The difference remained significant after adjusting for age, diabetic severity, and lifetime alcohol history (Table 18-15(f): p=0.029, Adj. RR=2.73). Contrasts between the background, low, and low plus high Ranch Hands and the Comparison group were nonsignificant in both the unadjusted and adjusted analyses (Table 18-15(e,f): p>0.13).

Neither the Model 4 unadjusted nor the adjusted analysis of diabetics detected a significant association between dorsalis pedis pulses and current dioxin (Table 18-15(g,h): p>0.18 for both analyses). Lifetime histories of cigarette smoking and alcohol use as well as family history of heart disease were significant covariates. In the Model 5 and 6 unadjusted analyses, the current dioxin effect was nonsignificant (Table 18-15(g): p>0.60 for both analyses). The interaction of current dioxin and lifetime cigarette smoking was significant in both the Model 5 and 6 adjusted analyses (Table 18-15: p=0.007 for Model 5 and p=0.008 for Model 6). Appendix Table N-2-7 shows the results stratified by smoking history for these interactions. The association between current dioxin and dorsalis pedis pulses was marginally significant for Ranch Hands who never smoked (Appendix Table N-2-7(a,b): p=0.081, Adj. RR=2.33 for Model 5 and p=0.098, Adj. RR=2.25, for Model 6) but was nonsignificant when cholesterol was removed from the final model (Table N-4-1(a,b): p=0.121 for Model 5 and p=0.134 for Model 6). For both Models 5 and 6, significant covariates were diabetic severity, lifetime alcohol history, family history of heart disease, and cholesterol.

Posterior Tibial Pulses (Doppler) (Diabetics)

In Model 1, the unadjusted and adjusted analyses of posterior tibial pulses in diabetics did not reveal a significant difference between Ranch Hands and Comparisons (Table 18-16(a,b): p>0.26 for all analyses). Significant covariates retained in the adjusted analysis included age, body fat, and current cigarette smoking.

In the Model 2 analysis of posterior tibial pulses in diabetics, neither the unadjusted nor the adjusted analysis revealed a significant association with initial dioxin (Table 18-16(c,d): p>0.31 for both analyses). Diabetic severity was the only significant covariate.

The contrast involving the high Ranch Hand category and the Comparison group was marginally significant in the Model 3 unadjusted analysis of posterior tibial pulses in diabetes (Table 18-16(e): p=0.079, Est. RR=2.87). The remaining three contrasts were nonsignificant (p>0.13). The difference between the high Ranch Hand category and the Comparison group remained marginally significant after adjusting for age, race, diabetic severity, and current cigarette smoking (Table 18-16(f): p=0.062, Adj. RR=3.45).

The relationship between current dioxin and posterior tibial pulses in diabetics was not significant in any of the Model 4 through 6 unadjusted and adjusted analyses (Table 18-16: p>0.58 for all analyses). Diabetic severity and lifetime cigarette smoking history were significant in each of the three adjusted analyses.

Table 18-16.
Analysis of Posterior Tibial Pulses (Doppler) (Diabetics)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Percent Abnormal	Est. Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*142*	*9.2*	*1.54 (0.67,3.55)*	*0.421*
	Comparison	*179*	*6.1*		
Officer	Ranch Hand	55	12.7	2.67 (0.65,10.92)	0.279
	Comparison	58	5.2		
Enlisted Flyer	Ranch Hand	25	4.0	0.33 (0.03,3.18)	0.602
	Comparison	36	11.1		
Enlisted Groundcrew	Ranch Hand	62	8.1	1.78 (0.46,6.91)	0.624
	Comparison	85	4.7		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks[a]
All	*1.37 (0.53,3.51)*	*0.519*	AGE (p=0.004)
Officer	2.35 (0.50,11.13)	0.281	BFAT (p=0.013)
Enlisted Flyer	0.25 (0.02,2.78)	0.262	DIABSEV (p=0.180)
Enlisted Groundcrew	1.84 (0.41,8.21)	0.425	CSMOK (p=0.085)

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 18-16. (Continued)
Analysis of Posterior Tibial Pulses (Doppler) (Diabetics)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	31	9.7	0.84 (0.51,1.37)	0.463
Medium	31	16.1		
High	34	5.9		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
96	0.76 (0.43,1.34)	0.317	DIABSEV (p=0.065)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 18-16. (Continued)
Analysis of Posterior Tibial Pulses (Doppler) (Diabetics)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	**n**	**Percent Abnormal**	**Est. Relative Risk (95% C.I.)[ab]**	**p-Value**
Comparison	148	4.7		
Background RH	42	4.8	0.83 (0.16,4.34)	0.829
Low RH	49	8.2	1.61 (0.44,5.83)	0.471
High RH	47	12.8	2.87 (0.89,9.32)	0.079
Low plus High RH	96	10.4	2.18 (0.78,6.05)	0.136

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	**n**	**Adj. Relative Risk (95% C.I.)[ac]**	**p-Value**	**Covariate Remarks**
Comparison	148			AGE (p=0.001) RACE (p=0.113) DIABSEV (p=0.193) CSMOK (p=0.046)
Background RH	42	0.43 (0.06,3.00)	0.395	
Low RH	49	1.18 (0.30,4.75)	0.812	
High RH	47	3.45 (0.94,12.61)	0.062	
Low plus High RH	96	1.98 (0.67,5.90)	0.218	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 18-16. (Continued)
Analysis of Posterior Tibial Pulses (Doppler) (Diabetics)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Abnormal/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	3.6 (28)	8.9 (56)	11.1 (54)	0.99 (0.67,1.45)	0.943
5	3.8 (26)	9.3 (54)	10.3 (58)	1.03 (0.74,1.42)	0.874
6[c]	3.8 (26)	9.3 (54)	10.3 (58)	0.98 (0.68,1.41)	0.899

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	138	1.04 (0.69,1.56)	0.860	DIABSEV (p=0.026) PACKYR (p=0.067)
5	138	1.09 (0.79,1.51)	0.587	DIABSEV (p=0.025) PACKYR (p=0.060)
6[d]	138	1.09 (0.79,1.51)	0.587	DIABSEV (p=0.025) PACKYR (p=0.060)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Leg Pulses (Doppler) (Diabetics)

No significant overall or stratified differences between Ranch Hands and Comparisons were revealed in the unadjusted and adjusted Model 1 analyses of leg pulses restricted to diabetics (Table 18-17(a,b): p>0.19 for all analyses). In the adjusted analysis, age, body fat, lifetime cigarette smoking history, cholesterol, and family history of heart disease were significant covariates.

Leg pulses were not significantly associated with initial dioxin in the Model 2 analyses of diabetics (Table 18-17(c,d): p>0.29 for both analyses). Family history of heart disease was the only significant covariate in the Model 2 adjusted analysis.

Both the unadjusted and adjusted Model 3 analyses revealed a significant dioxin effect for the contrast involving high Ranch Hands and Comparisons, restricted to diabetics. The relative risk for high Ranch Hands was greater than 3.00 for both unadjusted and adjusted analyses (Table 18-17(e,f): p=0.009, Est. RR=3.05, p=0.013, Adj. RR=3.07 respectively). The percentage of diabetic Ranch Hands in the high category with abnormal leg pulses was 29.8 percent compared to 12.8 percent for the Comparisons. Significant covariates included age and lifetime alcohol history.

None of the Model 4 through 6 unadjusted analyses on diabetics revealed a significant association between leg pulses and current dioxin (Table 18-17(g): p>0.47 for all analyses). The adjusted Model 4 analysis also had nonsignificant results (Table 18-17(h): p=0.263). For Model 5, the interaction of current dioxin and lifetime cigarette smoking history was significant (Table 18-17(h): p=0.026). Results from additional investigation on this interaction are found in Appendix Table N-2-8. The current dioxin effect was nonsignificant once the interaction was deleted from the final model (Table 18-17(h): p=0.271). The Model 6 adjusted analysis did not reveal a significant relationship between current dioxin and leg pulses in diabetics (p=0.391). Diabetic severity and lifetime alcohol history were retained in each of the three adjusted analyses. In addition, family history of heart disease was significant in the Model 5 analysis.

Peripheral Pulses (Doppler) (Diabetics)

Neither the unadjusted nor the adjusted Model 1 analysis of peripheral pulses in diabetics revealed significant results (Table 18-18(a,b): p>0.19 for all analyses). Significant covariates included age, body fat, lifetime alcohol history, and cholesterol.

Peripheral pulses were not significantly associated with initial dioxin in either analysis for Model 2, restricted to diabetics (Table 18-18(c,d): p>0.29 for both the unadjusted and adjusted analyses). Family history of heart disease was significant in the adjusted analysis.

In the Model 3 unadjusted analysis of peripheral pulses in diabetics, a significant difference between the high Ranch Hand category and the Comparison group was shown, with 29.8 percent of the high Ranch Hands and 13.5 percent of the Comparisons having abnormal peripheral pulses (Table 18-18(e): p=0.013, Est. RR=2.86). After adjusting for age, diabetic severity, and lifetime alcohol history, the difference between high Ranch Hands and

Table 18-17.
Analysis of Leg Pulses (Doppler) (Diabetics)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Percent Abnormal	Est. Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*142*	*18.3*	*1.45 (0.79,2.65)*	*0.295*
	Comparison	*179*	*13.4*		
Officer	Ranch Hand	55	18.2	1.62 (0.56,4.61)	0.519
	Comparison	58	12.1		
Enlisted Flyer	Ranch Hand	25	12.0	0.56 (0.13,2.44)	0.674
	Comparison	36	19.4		
Enlisted Groundcrew	Ranch Hand	62	21.0	1.99 (0.81,4.89)	0.198
	Comparison	85	11.8		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks[a]
All	*1.17 (0.59,2.32)*	*0.661*	AGE (p=0.045)
			BFAT (p=0.010)
Officer	1.41 (0.45,4.44)	0.554	DIABSEV (p=0.341)
Enlisted Flyer	0.49 (0.10,2.31)	0.366	PACKYR (p=0.140)
			CHOL (p=0.128)
Enlisted Groundcrew	1.51 (0.53,4.29)	0.435	HRTDIS (p=0.066)

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 18-17. (Continued)
Analysis of Leg Pulses (Doppler) (Diabetics)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	31	9.7	1.20 (0.85,1.70)	0.294
Medium	31	25.8		
High	34	23.5		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
96	1.19 (0.82,1.73)	0.366	DIABSEV (p=0.399) HRTDIS (p=0.039)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 18-17. (Continued)
Analysis of Leg Pulses (Doppler) (Diabetics)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	148	12.8		
Background RH	42	14.3	0.92 (0.33,2.59)	0.875
Low RH	49	10.2	0.66 (0.23,1.92)	0.444
High RH	47	29.8	3.05 (1.32,7.02)	0.009
Low plus High RH	96	19.8	1.56 (0.76,3.21)	0.224

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	145			AGE (p=0.042) DIABSEV (p=0.271) DRKYR (p=0.035)
Background RH	42	0.56 (0.17,1.88)	0.348	
Low RH	47	0.39 (0.11,1.34)	0.134	
High RH	46	3.07 (1.27,7.47)	0.013	
Low plus High RH	93	1.31 (0.61,2.80)	0.486	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 18-17. (Continued)
Analysis of Leg Pulses (Doppler) (Diabetics)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Abnormal/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	17.9 (28)	8.9 (56)	27.8 (54)	1.11 (0.84,1.46)	0.476
5	19.2 (26)	9.3 (54)	25.9 (58)	1.07 (0.84,1.35)	0.585
6[c]	19.2 (26)	9.3 (54)	25.9 (58)	1.06 (0.81,1.38)	0.677

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	135	1.20 (0.87,1.66)	0.263	DIABSEV (p=0.008) DRKYR (p=0.028)
5	133	1.16 (0.89,1.52)**	0.271**	CURR*PACKYR (p=0.026) DIABSEV (p=0.054) HRTDIS (p=0.050) DRKYR (p=0.069)
6[d]	135	1.14 (0.84,1.55)	0.391	DIABSEV (p=0.010) DRKYR (p=0.026)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table N-2-8 for further analysis of this interaction.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 18-18.
Analysis of Peripheral Pulses (Doppler) (Diabetics)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Abnormal**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	*Ranch Hand*	*142*	*19.0*	*1.45 (0.80,2.62)*	*0.286*
	Comparison	*179*	*14.0*		
Officer	Ranch Hand	55	20.0	1.56 (0.58,4.23)	0.529
	Comparison	58	13.8		
Enlisted Flyer	Ranch Hand	25	12.0	0.56 (0.13,2.44)	0.674
	Comparison	36	19.4		
Enlisted Groundcrew	Ranch Hand	62	21.0	1.99 (0.81,4.89)	0.198
	Comparison	85	11.8		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	*1.12 (0.58,2.18)*	*0.733*	AGE (p=0.007) BFAT (p=0.003) DIABSEV (p=0.164) DRKYR (p=0.023) CHOL (p=0.086)
Officer	1.39 (0.47,4.06)	0.553	
Enlisted Flyer	0.49 (0.10,2.27)	0.359	
Enlisted Groundcrew	1.40 (0.50,3.90)	0.524	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 18-18. (Continued)
Analysis of Peripheral Pulses (Doppler) (Diabetics)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	31	9.7	1.20 (0.85,1.70)	0.294
Medium	31	25.8		
High	34	23.5		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
96	1.19 (0.82,1.73)	0.366	DIABSEV (p=0.399) HRTDIS (p=0.039)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 18-18. (Continued)
Analysis of Peripheral Pulses (Doppler) (Diabetics)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	**n**	**Percent Abnormal**	**Est. Relative Risk (95% C.I.)[ab]**	**p-Value**
Comparison	148	13.5		
Background RH	42	16.7	1.05 (0.39,2.81)	0.919
Low RH	49	10.2	0.62 (0.21,1.79)	0.376
High RH	47	29.8	2.86 (1.25,6.55)	0.013
Low plus High RH	96	19.8	1.47 (0.72,3.00)	0.292

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	**n**	**Adj. Relative Risk (95% C.I.)[ac]**	**p-Value**	**Covariate Remarks**
Comparison	145			AGE (p=0.012) DIABSEV (p=0.239) DRKYR (p=0.063)
Background RH	42	0.70 (0.23,2.17)	0.539	
Low RH	47	0.35 (0.10,1.22)	0.099	
High RH	46	2.95 (1.21,7.16)	0.017	
Low plus High RH	93	1.22 (0.57,2.60)	0.605	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 18-18. (Continued)
Analysis of Peripheral Pulses (Doppler) (Diabetics)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Abnormal/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	21.4 (28)	8.9 (56)	27.8 (54)	1.07 (0.81,1.41)	0.631
5	23.1 (26)	9.3 (54)	25.9 (58)	1.04 (0.82,1.31)	0.746
6[c]	23.1 (26)	9.3 (54)	25.9 (58)	1.03 (0.79,1.34)	0.834

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	133	****	****	CURR*HRTDIS (p=0.005) DIABSEV (p=0.016) DRKYR (p=0.033)
5	135	1.12 (0.86,1.44)	0.399	DIABSEV (p=0.015) DRKYR (p=0.031)
6[d]	133	1.10 (0.81,1.49)**	0.534**	CURR*HRTDIS (p=0.014) DIABSEV (p=0.022) DRKYR (p=0.032)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table N-2-9 for further analysis of this interaction.

**** Log_2 (current dioxin + 1)-by-covariate interaction ($p \leq 0.01$); adjusted relative risk, confidence interval, and p-value not presented; refer to Appendix Table N-2-9 for further analysis of this interaction.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Comparisons remained significant (Table 18-18(f): p=0.017, Adj. RR=2.95). In addition, the contrast involving low Ranch Hands and Comparisons was marginally significant in the adjusted analysis, with an adjusted relative risk less than one (p=0.099, Adj. RR=0.35).

For Models 4 through 6, the unadjusted analyses of peripheral pulses in diabetics did not reveal significant results (Table 18-18(g): p>0.63 for all analyses). In the adjusted Model 4 analysis, a highly significant interaction between current dioxin and family history of heart disease was revealed (Table 18-18(h): p=0.005). This interaction is further explored in Appendix Table N-2-9. The results in the Model 5 adjusted analysis were nonsignificant (p=0.399). Adjustment in the whole-weight current dioxin measurement for total lipids led to a significant interaction between current dioxin and family history of heart disease in Model 6 (Table 18-18(h): p=0.014). However, after removing the interaction from the final model, the association between peripheral pulses in diabetics and current dioxin was not significant (p=0.534). Appendix Table N-2-9 shows further analysis stratified by family history of heart disease (yes, no). Each of the three adjusted analyses retained diabetic severity and lifetime alcohol history.

Thyroid Stimulating Hormone (Continuous)

The Model 1 unadjusted and adjusted analyses of thyroid stimulating hormone (TSH) in its continuous form did not show a statistically significant difference in mean TSH levels between Ranch Hands and Comparisons (Table 18-19(a,b): p>0.26 for all analyses). Significant covariates included age, race, and occupation.

Both the unadjusted and adjusted analyses of Models 2 and 3 showed nonsignificant relationships between dioxin and TSH measured continuously (Table 18-19(c-f): p>0.10 for all analyses). In the Model 2 adjusted analysis, race was the only significant covariate, whereas in the Model 3 analysis, age, race, and occupation were significant.

None of the unadjusted analyses detected a significant association between current dioxin and TSH for Models 4 through 6 (Table 18-19(g): p>0.33 for all analyses). The adjusted Model 4 and Model 6 analyses also had nonsignificant results (Table 18-19(h): p>0.10 for both analyses). However, a marginally significant positive relationship between current dioxin and TSH was shown in the adjusted analysis for Model 5 (Table 18-19(h): p=0.056, Slope=0.0265). But, when occupation was removed from the final model, the relationship between current dioxin and TSH became nonsignificant (Table N-3-9(b): p=0.345). Race and occupation were significant covariates in each of the adjusted analyses.

Thyroid Stimulating Hormone (Discrete)

The frequencies of Ranch Hands and Comparisons with abnormally high TSH levels were not significantly different in either the unadjusted or adjusted Model 1 analyses (Table 18-20(a,b): p>0.27 for all contrasts). Age and race were determined to be significant covariates in the adjusted model.

A marginally significant association between TSH and initial dioxin was revealed in the unadjusted Model 2 analysis (Table 18-20(c): Est. RR=1.44, p=0.076). In both the low and

Table 18-19.
Analysis of Thyroid Stimulating Hormone (TSH) (μIU/ml) (Continuous)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	*Ranch Hand*	*932*	*1.62*	*0.05 --*	*0.275*
	Comparison	*1,237*	*1.57*		
Officer	Ranch Hand	357	1.73	0.08 --	0.269
	Comparison	480	1.65		
Enlisted Flyer	Ranch Hand	158	1.47	-0.04 --	0.710
	Comparison	198	1.51		
Enlisted Groundcrew	Ranch Hand	417	1.59	0.06 --	0.367
	Comparison	559	1.53		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Group	n	Adj. Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]	Covariate Remarks[d]
All	*Ranch Hand*	*932*	*1.41*	*0.04 --*	0.282	AGE (p<0.001)
	Comparison	*1,237*	*1.37*			RACE (p<0.001)
Officer	Ranch Hand	357	1.47	0.07 --	0.280	OCC (p=0.044)
	Comparison	480	1.40			
Enlisted Flyer	Ranch Hand	158	1.28	-0.04 --	0.645	
	Comparison	198	1.32			
Enlisted Groundcrew	Ranch Hand	417	1.44	0.05 --	0.377	
	Comparison	559	1.39			

[a] Transformed from the natural logarithm scale.

[b] Difference of means after transformation to original scale; confidence interval on difference of means not given because analysis was performed on natural logarithm scale.

[c] P-values based on difference of means on natural logarithm scale.

[d] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 18-19. (Continued)
Analysis of Thyroid Stimulating Hormone (TSH) (μIU/ml) (Continuous)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	170	1.58	1.58	0.005	0.0043 (0.0215)	0.841
Medium	171	1.58	1.58			
High	168	1.70	1.69			

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED						
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[d]			
Initial Dioxin	n	Adj. Mean[ad]	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
Low	170	1.34	0.032	-0.0017 (0.0213)	0.937	RACE ($p<0.001$)
Medium	171	1.32				
High	168	1.41				

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Slope and standard error based on natural logarithm of TSH versus $\log_2$ (initial dioxin).

[d] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 18-19. (Continued)
Analysis of Thyroid Stimulating Hormone (TSH) (μIU/ml)
(Continuous)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED					
Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,027	1.58	1.58		
Background RH	365	1.64	1.64	0.07 --	0.293
Low RH	254	1.60	1.60	0.02 --	0.777
High RH	255	1.64	1.64	0.06 --	0.376
Low plus High RH	509	1.62	1.62	0.04 --	0.450

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED					
Dioxin Category	n	Adj. Mean[ae]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]	Covariate Remarks
Comparison	1,027	1.36			AGE (p=0.003) RACE (p<0.001) OCC (p=0.031)
Background RH	365	1.37	0.02 --	0.739	
Low RH	254	1.38	0.03 --	0.655	
High RH	255	1.46	0.10 --	0.105	
Low plus High RH	509	1.42	0.06 --	0.175	

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Difference of adjusted means after transformation to original scale; confidence interval on difference of adjusted means not given because analysis was performed on natural logarithm scale.

[d] P-value is based on difference of means on natural logarithm scale.

[e] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 18-19. (Continued)
Analysis of Thyroid Stimulating Hormone (TSH) (μIU/ml)
(Continuous)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED						
	Current Dioxin Category Mean[a]/(n)			Analysis Results for Log_2 (Current Dioxin + 1)		
Model[b]	Low	Medium	High	R^2	Slope (Std. Error)[c]	p-Value
4	1.61 (291)	1.65 (290)	1.63 (293)	<0.001	0.0087 (0.0145)	0.547
5	1.59 (296)	1.64 (288)	1.65 (290)	0.001	0.0120 (0.0124)	0.334
6[d]	1.61 (295)	1.64 (288)	1.63 (290)	0.003	0.0060 (0.0134)	0.655

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED							
	Current Dioxin Category Adjusted Mean[a]/(n)			Analysis Results for Log_2 (Current Dioxin + 1)			
Model[b]	Low	Medium	High	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
4	1.30 (291)	1.39 (290)	1.42 (293)	0.029	0.0265 (0.0165)	0.108	RACE (p<0.001) OCC (p=0.021)
5	1.29 (296)	1.39 (288)	1.44 (290)	0.030	0.0265 (0.0139)	0.056	RACE (p<0.001) OCC (p=0.016)
6[e]	1.30 (295)	1.39 (288)	1.43 (290)	0.031	0.0233 (0.0150)	0.121	RACE (p<0.001) OCC (p=0.018)

[a] Transformed from natural logarithm scale.

[b] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[c] Slope and standard error based on natural logarithm of TSH versus log_2 (current dioxin +1).

[d] Adjusted for log_2 total lipids.

[e] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 18-20.
Analysis of Thyroid Stimulating Hormone (TSH)
(Discrete)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Abnormal High**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***932***	***2.4***	***1.01 (0.57,1.76)***	***0.999***
	Comparison	***1,237***	***2.3***		
Officer	Ranch Hand	357	2.2	0.62 (0.27,1.46)	0.374
	Comparison	480	3.5		
Enlisted Flyer	Ranch Hand	158	2.5	2.55 (0.46,14.08)	0.488
	Comparison	198	1.0		
Enlisted Groundcrew	Ranch Hand	417	2.4	1.35 (0.56,3.27)	0.663
	Comparison	559	1.8		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***1.00 (0.57,1.75)***	***0.999***	AGE (p=0.079) RACE (p=0.015)
Officer	0.62 (0.26,1.46)	0.273	
Enlisted Flyer	2.50 (0.45,13.87)	0.294	
Enlisted Groundcrew	1.35 (0.55,3.27)	0.512	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 18-20. (Continued)
Analysis of Thyroid Stimulating Hormone (TSH)
(Discrete)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Abnormal High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	170	1.2	1.44 (0.97,2.15)	0.076
Medium	171	1.2		
High	168	4.8		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[a]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
509	1.44 (0.97,2.15)	0.076	

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 18-20. (Continued)
Analysis of Thyroid Stimulating Hormone (TSH)
(Discrete)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	**n**	**Percent Abnormal High**	**Est. Relative Risk (95% C.I.)[ab]**	**p-Value**
Comparison	1,027	2.4		
Background RH	365	2.5	0.93 (0.43,2.02)	0.847
Low RH	254	1.2	0.49 (0.15,1.64)	0.246
High RH	255	3.5	1.59 (0.73,3.47)	0.245
Low plus High RH	509	2.4	1.02 (0.50,2.05)	0.964

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	**n**	**Adj. Relative Risk (95% C.I.)[ac]**	**p-Value**	**Covariate Remarks**
Comparison	1,027			AGE (p=0.145) RACE (p=0.029)
Background RH	365	0.88 (0.40,1.92)	0.753	
Low RH	254	0.50 (0.15,1.67)	0.260	
High RH	255	1.72 (0.78,3.80)	0.176	
Low plus High RH	509	1.06 (0.53,2.15)	0.862	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin $\leq$ 10 ppt.
Background (Ranch Hand): Current Dioxin $\leq$ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin $\leq$ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 18-20. (Continued)
Analysis of Thyroid Stimulating Hormone (TSH)
(Discrete)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

	Current Dioxin Category Percent Abnormal High/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	2.4 (291)	1.7 (290)	3.1 (293)	1.15 (0.87,1.53)	0.327
5	2.0 (296)	2.1 (288)	3.1 (290)	1.16 (0.90,1.50)	0.242
6[c]	2.0 (295)	2.1 (288)	3.1 (290)	1.12 (0.85,1.47)	0.428

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	874	1.15 (0.87,1.52)	0.330	RACE (p=0.111)
5	874	1.16 (0.90,1.48)	0.252	RACE (p=0.114)
6[d]	873	1.16 (0.90,1.49)	0.257	RACE (p=0.114)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

medium categories of initial dioxin, 1.2 percent of the participants had abnormally high TSH levels in contrast to 4.8 percent in the high category. In the adjusted analysis, no covariates were retained; therefore, the results of this analysis were identical to those of the unadjusted analysis.

For Model 3, no significant differences were evident between the four Ranch Hand categories and the Comparison group in the unadjusted and adjusted analyses of discrete TSH (Table 18-20(e,f): p>0.17 for all contrasts). Age and race were significant covariates in the adjusted analysis.

No significant results were revealed in the Model 4 through 6 unadjusted and adjusted analyses of discrete TSH versus current dioxin (Table 18-20(g,h): p>0.24 for all analyses). Race was retained in each of the three adjusted analyses.

Thyroxine (Continuous)

No significant group effect was detected in the unadjusted and adjusted Model 1 analyses of thyroxine (T_4) (Table 18-21(a,b): p>0.22 for all contrasts). Covariates retained in the adjusted analysis were age and occupation.

For Model 2 neither the unadjusted nor the adjusted analyses of thyroxine detected a significant association with initial dioxin (Table 18-21(c,d): p>0.28 for both analyses). Race and occupation were significant covariates.

Likewise, for Model 3, there were no significant differences between Ranch Hands and Comparisons in either analysis (Table 18-21(e,f): p>0.14 for both the unadjusted and the adjusted contrasts). Age, occupation, and the race-by-personality type interaction were significant in the adjusted analysis.

In the Model 4 unadjusted analysis, a marginally significant positive association between current dioxin and thyroxine was revealed (Table 18-21(g): p=0.085, Slope=0.0532). However, after adjusting for race, occupation, and personality type, the association became nonsignificant (Table 18-21(h): p=0.515). The relationship between thyroxine and current dioxin was not significant in the Models 5 and 6 unadjusted and adjusted analyses (Table 18-21(g,h): p>0.10 for Models 5 and 6). Race, occupation, and personality type were retained in both adjusted analyses.

Thyroxine (Discrete)

In the Model 1 unadjusted analysis of thyroxine, the percentage of Ranch Hands with abnormally low levels of thyroxine did not differ significantly from the percentage of Comparisons (Table 18-22(a): p=0.999). The difference remained nonsignificant after adjusting for occupation (Table 18-22(b): p=0.996). Analysis within the three occupational categories was performed only for the officer stratum because of the sparse number of abnormalities in the remaining two occupational strata. Only one enlisted flyer Ranch Hand and three enlisted groundcrew Comparisons had abnormally low thyroxine levels. For

Table 18-21.
Analysis of Thyroxine (T_4) ($\mu g/dl$)
(Continuous)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Mean	Difference of Means (95% C.I.)	p-Value
All	*Ranch Hand*	*932*	*7.79*	*-0.04 (-0.15,0.07)*	*0.499*
	Comparison	*1,237*	*7.83*		
Officer	Ranch Hand	357	7.50	-0.11 (-0.28,0.07)	0.224
	Comparison	480	7.61		
Enlisted Flyer	Ranch Hand	158	7.97	0.02 (-0.24,0.28)	0.877
	Comparison	198	7.95		
Enlisted Groundcrew	Ranch Hand	417	7.98	-0.01 (-0.18,0.17)	0.948
	Comparison	559	7.98		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Group	n	Adj. Mean	Difference of Adj. Means (95% C.I.)	p-Value	Covariate Remarks[a]
All	*Ranch Hand*	*932*	*7.81*	*-0.04 (-0.15,0.07)*	0.456	AGE (p=0.044)
	Comparison	*1,237*	*7.85*			OCC (p<0.001)
Officer	Ranch Hand	357	7.48	-0.11 (-0.29,0.07)	0.224	
	Comparison	480	7.59			
Enlisted Flyer	Ranch Hand	158	7.96	0.02 (-0.26,0.29)	0.892	
	Comparison	198	7.94			
Enlisted Groundcrew	Ranch Hand	417	8.00	-0.01 (-0.17,0.16)	0.945	
	Comparison	559	8.01			

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 18-21. (Continued)
Analysis of Thyroxine (T_4) (μg/dl)
(Continuous)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[a]		
Initial Dioxin	n	Mean	Adj. Mean[a]	R^2	Slope (Std. Error)	p-Value
Low	170	7.84	7.85	0.008	0.0465 (0.0432)	0.282
Medium	171	7.73	7.73			
High	168	7.97	7.96			

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED						
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[b]			
Initial Dioxin	n	Adj. Mean[b]	R^2	Adj. Slope (Std. Error)	p-Value	Covariate Remarks
Low	170	7.72	0.023	-0.0101 (0.0500)	0.839	RACE (p=0.060) OCC (p=0.069)
Medium	171	7.49				
High	168	7.64				

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 18-21. (Continued)
Analysis of Thyroxine (T_4) (μg/dl)
(Continuous)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Mean	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)	p-Value
Comparison	1,027	7.80	7.80		
Background RH	365	7.68	7.70	-0.10 (-0.26,0.06)	0.218
Low RH	254	7.86	7.85	0.05 (-0.14,0.23)	0.617
High RH	255	7.84	7.82	0.02 (-0.16,0.20)	0.831
Low plus High RH	509	7.85	7.83	0.03 (-0.11,0.17)	0.646

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Mean[b]	Difference of Adj. Mean vs. Comparisons (95% C.I.)	p-Value	Covariate Remarks
Comparison	1,026	7.75			AGE (p=0.147) OCC (p<0.001) RACE*PERS (p=0.048)
Background RH	365	7.76	0.01 (-0.15,0.17)	0.874	
Low RH	253	7.79	0.04 (-0.14,0.22)	0.645	
High RH	255	7.61	-0.14 (-0.32,0.05)	0.143	
Low plus High RH	508	7.70	-0.05 (-0.19,0.09)	0.500	

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 18-21. (Continued)
Analysis of Thyroxine (T_4) ($\mu g/dl$)
(Continuous)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED						
	Current Dioxin Category Mean/(n)			Analysis Results for Log_2 (Current Dioxin + 1)		
Model[a]	Low	Medium	High	R^2	Slope (Std. Error)	p-Value
4	7.70 (291)	7.82 (290)	7.82 (293)	0.003	0.0532 (0.0308)	0.085
5	7.74 (296)	7.74 (288)	7.85 (290)	0.002	0.0384 (0.0264)	0.147
6[b]	7.73 (295)	7.74 (288)	7.86 (290)	0.003	0.0469 (0.0286)	0.101

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED							
	Current Dioxin Category Adjusted Mean/(n)			Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	Low	Medium	High	R^2	Adj. Slope (Std. Error)	p-Value	Covariate Remarks
4	7.67 (291)	7.70 (289)	7.48 (293)	0.030	-0.0228 (0.0350)	0.515	RACE (p=0.061) OCC (p<0.001) PERS (p=0.125)
5	7.71 (296)	7.63 (287)	7.53 (290)	0.030	-0.0243 (0.0295)	0.411	RACE (p=0.058) OCC (p<0.001) PERS (p=0.126)
6[c]	7.71 (295)	7.63 (287)	7.53 (290)	0.031	-0.0215 (0.0320)	0.503	RACE (p=0.053) OCC (p<0.001) PERS (p=0.143)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Adjusted for log_2 total lipids.

[c] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 18-22.
Analysis of Thyroxine (T_4)
(Discrete)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Abnormal Low**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***932***	***0.6***	***1.00 (0.34,2.88)***	***0.999***
	Comparison	***1,237***	***0.6***		
Officer	Ranch Hand	357	1.4	1.35 (0.39,4.70)	0.880
	Comparison	480	1.0		
Enlisted Flyer	Ranch Hand	158	0.6	--	--
	Comparison	198	0.0		
Enlisted Groundcrew	Ranch Hand	417	0.0	--	--
	Comparison	559	0.5		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***1.00 (0.35,2.91)***	***0.996***	OCC (p=0.044)
Officer	1.35 (0.39,4.70)	0.880	
Enlisted Flyer	--	--	
Enlisted Groundcrew	--	--	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

--: Adjusted relative risk, confidence interval, and p-value not presented due to the sparse number of abnormalities.

Table 18-22. (Continued)
Analysis of Thyroxine (T_4)
(Discrete)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Abnormal Low	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	170	0.0	1.06 (0.43,2.57)	0.903
Medium	171	1.2		
High	168	0.6		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
509	6.55 (1.02,42.10)	0.028	OCC (p=0.004)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 18-22. (Continued)
Analysis of Thyroxine (T_4)
(Discrete)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	**n**	**Percent Abnormal Low**	**Est. Relative Risk (95% C.I.)[ab]**	**p-Value**
Comparison	1,027	0.8		
Background RH	365	0.5	0.74 (0.16,3.56)	0.712
Low RH	254	0.4	0.47 (0.06,3.83)	0.484
High RH	255	0.8	0.95 (0.20,4.55)	0.947
Low plus High RH	509	0.6	0.71 (0.19,2.71)	0.617

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	**n**	**Adj. Relative Risk (95% C.I.)[ac]**	**p-Value**	**Covariate Remarks**
Comparison	1,027			OCC (p=0.039)
Background RH	365	0.52 (0.11,2.54)	0.423	
Low RH	254	0.45 (0.06,3.69)	0.459	
High RH	255	2.15 (0.36,12.81)	0.400	
Low plus High RH	509	0.91 (0.23,3.57)	0.895	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 18-22. (Continued)
Analysis of Thyroxine (T_4)
(Discrete)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Abnormal Low/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	0.3 (291)	0.7 (290)	0.7 (293)	1.08 (0.60,1.95)	0.789
5	0.3 (296)	0.7 (288)	0.7 (290)	1.13 (0.68,1.89)	0.639
6[c]	0.3 (295)	0.7 (288)	0.7 (290)	1.05 (0.60,1.83)	0.868

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	874	3.22 (1.08,9.63)	0.030	OCC (p=0.004)
5	874	2.60 (1.11,6.10)	0.025	OCC (p=0.004)
6[d]	873	2.83 (0.97,8.24)	0.043	OCC (p=0.005)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

officers, there was no significant difference between Ranch Hands and Comparisons in either the unadjusted or adjusted analyses (Table 18-22(a,b): p=0.880 for both contrasts).

The unadjusted analyses for Models 2 and 3 did not show a significant association between discrete thyroxine and dioxin (Table 18-22(c,e): p>0.48 for all analyses). Adjusting for occupation in the Model 2 analysis led to a significant initial dioxin effect (Table 18-22(d): p=0.028, Adj. RR=6.55). However, for the Model 3 analysis, adjusting for occupation did not reveal a significant association between thyroxine and categorized dioxin (Table 18-22(f): p≥0.40 for all contrasts).

None of the Model 4 through 6 unadjusted analyses detected a significant association between discrete thyroxine and current dioxin (Table 18-22(g): p>0.63 for all analyses). However, adjustment for occupation led to a significant dioxin effect in each of the three adjusted analyses, the relative risk being greater than 2.5 in each case (Table 18-22(h): p=0.030, Adj. RR=3.22 for Model 4; p=0.025, Adj. RR=2.60 for Model 5; and p=0.043, Adj. RR=2.83 for Model 6).

Anti-Thyroid Antibodies

The overall unadjusted contrast for Ranch Hands versus Comparisons was marginally significant in the Model 1 analysis of anti-thyroid antibodies (Table 18-23(a): p=0.071, Est. RR=1.62). In the Ranch Hand category, 3.9 percent had anti-thyroid antibodies present in contrast to 2.4 percent for the Comparison group. When investigated within the three occupational levels, however, the difference was nonsignificant (p>0.18 for all contrasts). No covariates were retained in the adjusted analysis; therefore, these results are identical to those of the unadjusted analysis.

In the Model 2 analyses of anti-thyroid antibodies, the association with initial dioxin was not significant (Table 18-23(c,d): p>0.54 for both the unadjusted and adjusted analyses). The age-by-personality type interaction was significant for the adjusted model.

For Model 3, significant differences between both low and low plus high Ranch Hands and Comparisons were shown in the unadjusted analysis (Table 18-23(e): p=0.060, Est. RR=1.97, for low Ranch Hands vs. Comparisons and p=0.048, Est. RR=1.80 for low plus high Ranch Hands vs. Comparisons). In the dioxin categories, 4.7 percent of the low Ranch Hands and 4.3 percent of the low plus high Ranch Hands had anti-thyroid antibodies present compared to 2.4 percent of the Comparisons. The results of the adjusted analysis duplicated those of the unadjusted analysis because no covariates were significant.

None of the unadjusted and adjusted Model 4 through 6 analyses detected a significant association between current dioxin and the presence of anti-thyroid antibodies (Table 18-23(g,h): p>0.56 for all analyses). The age-by-personality type interaction was significant in each of the adjusted analyses.

Table 18-23.
Analysis of Anti-Thyroid Antibodies

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	Group	n	Percent Present	Est. Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*932*	*3.9*	*1.62 (0.99,2.64)*	*0.071*
	Comparison	*1,237*	*2.4*		
Officer	Ranch Hand	357	3.9	1.36 (0.64,2.89)	0.545
	Comparison	480	2.9		
Enlisted Flyer	Ranch Hand	158	4.4	3.01 (0.77,11.85)	0.183
	Comparison	198	1.5		
Enlisted Groundcrew	Ranch Hand	417	3.6	1.57 (0.74,3.33)	0.325
	Comparison	559	2.3		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks[a]
All	*1.62 (0.99,2.64)*	*0.071*	
Officer	1.36 (0.64,2.89)	0.545	
Enlisted Flyer	3.01 (0.77,11.85)	0.183	
Enlisted Groundcrew	1.57 (0.74,3.33)	0.325	

Table 18-23. (Continued)
Analysis of Anti-Thyroid Antibodies

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Present	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	170	5.3	0.92 (0.66,1.30)	0.644
Medium	171	3.5		
High	168	4.2		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
508	0.89 (0.62,1.29)	0.543	AGE*PERS (p=0.036)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 18-23. (Continued)
Analysis of Anti-Thyroid Antibodies

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Present	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,027	2.4		
Background RH	365	3.6	1.48 (0.74,2.94)	0.266
Low RH	254	4.7	1.97 (0.97,3.98)	0.060
High RH	255	3.9	1.64 (0.78,3.48)	0.195
Low plus High RH	509	4.3	1.80 (1.00,3.24)	0.048

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ab]	p-Value	Covariate Remarks
Comparison	1,027			
Background RH	365	1.48 (0.74,2.94)	0.266	
Low RH	254	1.97 (0.97,3.98)	0.060	
High RH	255	1.64 (0.78,3.48)	0.195	
Low plus High RH	509	1.80 (1.00,3.24)	0.048	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 18-23. (Continued)
Analysis of Anti-Thyroid Antibodies

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Present/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	3.4 (291)	4.8 (290)	3.8 (293)	1.03 (0.82,1.30)	0.776
5	3.0 (296)	5.2 (288)	3.8 (290)	1.06 (0.87,1.29)	0.563
6[c]	3.1 (295)	5.2 (288)	3.8 (290)	1.01 (0.82,1.26)	0.903

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	873	1.02 (0.80,1.30)	0.866	AGE*PERS (p=0.022)
5	873	1.05 (0.85,1.29)	0.644	AGE*PERS (p=0.024)
6[d]	872	1.00 (0.80,1.25)	0.999	AGE*PERS (p=0.022)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Fasting Glucose (All Participants—Continuous)

The difference in mean fasting glucose levels between Ranch Hands and Comparisons was not statistically significant in either the Model 1 unadjusted or adjusted analyses (Table 18-24(a,b): p>0.14 for all analyses). The race-by-occupation, age-by-race, age-by-body fat, and body fat-by-family history of diabetes interactions were retained in the adjusted analysis.

The association between fasting glucose and dioxin was not significant in either of the unadjusted analyses for Models 2 and 3 (Table 18-24(c,e): p>0.10 for all analyses). In the Model 2 adjusted analysis, a significant interaction between initial dioxin and occupation was revealed (Table 18-24(d): p=0.013). Appendix Table N-2-10 displays the results stratified by occupation. A highly significant dioxin effect remained after deleting the interaction from the final model (p=0.003, Slope=0.0248). The respective adjusted means for fasting glucose for the low, medium, and high categories of initial dioxin were 110.27 mg/dl, 112.56 mg/dl, and 117.28 mg/dl. Additional covariates retained in the adjusted analysis were age, race, body fat, and the personality type-by-family history of diabetes and occupation-by-family history of diabetes interactions.

Analogous to the Model 2 analysis, the interaction between categorized dioxin and occupation was significant in the Model 3 adjusted analysis (Table 18-24(f): p=0.015). Appendix Table N-2-10 contains additional information on this interaction. Removal of the interaction from the final model led to a marginally significant difference in mean fasting glucose levels between Ranch Hands in the high category and the Comparison group (p=0.067, Diff. of Adj. Means=2.74). The adjusted fasting glucose mean for high Ranch Hands was 110.16 mg/dl compared to 107.43 mg/dl for Comparisons. Family history of diabetes and the age-by-body fat and race-by-occupation interactions were significant in the adjusted analysis.

Each of the unadjusted Model 4 through 6 analyses detected a highly significant positive association between current dioxin and fasting glucose. For Model 4, the respective mean fasting glucose levels for the low, medium, and high categories of initial dioxin were 101.39 mg/dl, 105.70 mg/dl, and 106.41 mg/dl (Table 18-24(g): p<0.001, Slope=0.0185). For Model 5, the respective means were 101.34 mg/dl, 103.86 mg/dl, and 108.43 mg/dl (p<0.001, Slope=0.0193). For Model 6, after adjusting for total lipids, the respective means were 101.39 mg/dl, 103.86 mg/dl, and 108.43 mg/dl (p=0.005, Slope=0.0116). The Model 4 adjusted analysis of fasting glucose detected a highly significant positive association with current dioxin (Table 18-24(h): p<0.001, Slope=0.0217). Adjusted fasting glucose means were 103.01 mg/dl, 105.50 mg/dl, and 108.71 mg/dl for the low, medium, and high categories of current dioxin. In the Model 5 adjusted analysis, the interaction of current dioxin and body fat was significant (p=0.044). Further analysis of this interaction is found in Appendix Table N-2-10. After deleting the interaction from the final model, a highly significant dioxin effect remained (p<0.001, Slope=0.0214). For Model 5, the adjusted means for the low, medium, and high current dioxin categories were 102.71 mg/dl, 103.84 mg/dl, and 110.87 mg/dl. For the Model 6 adjusted analysis, the association between fasting glucose and current dioxin was again highly significant (p=0.005, Slope=0.0122). Adjusted means for fasting glucose in Model 6 were 106.81 mg/dl, 106.64 mg/dl, and 110.94 mg/dl for the low, medium, and high current dioxin categories. The age-by-body fat, occupation-by-family history of diabetes, and

Table 18-24.
Analysis of Fasting Glucose (mg/dl) (All Participants) (Continuous)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	*Ranch Hand*	*950*	*104.29*	*-0.05 --*	*0.954*
	Comparison	*1,277*	*104.34*		
Officer	Ranch Hand	365	105.13	1.12 --	0.414
	Comparison	502	104.01		
Enlisted Flyer	Ranch Hand	162	103.95	-3.49 --	0.149
	Comparison	202	107.44		
Enlisted Groundcrew	Ranch Hand	423	103.71	0.14 --	0.914
	Comparison	573	103.56		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Group	n	Adj. Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]	Covariate Remarks[d]
All	*Ranch Hand*	*932*	*107.69*	*0.01 --*	0.993	RACE*OCC (p=0.004)
	Comparison	*1,259*	*107.68*			AGE*RACE (p=0.030)
						AGE*BFAT (p=0.009)
Officer	Ranch Hand	359	101.25	0.81 --	0.540	BFAT*FAMDIAB (p=0.020)
	Comparison	499	100.44			
Enlisted Flyer	Ranch Hand	159	111.29	-3.13 --	0.167	
	Comparison	197	114.42			
Enlisted Groundcrew	Ranch Hand	414	109.74	0.38 --	0.779	
	Comparison	563	109.36			

[a] Transformed from the natural logarithm scale.

[b] Difference of means after transformation to original scale; confidence interval on difference of means not given because analysis was performed on natural logarithm scale.

[c] P-values based on difference of means on natural logarithm scale.

[d] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 18-24. (Continued)
Analysis of Fasting Glucose (mg/dl) (All Participants) (Continuous)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED						
Initial Dioxin Category Summary Statistics				**Analysis Results for Log_2 (Initial Dioxin)[b]**		
Initial Dioxin	**n**	**Mean[a]**	**Adj. Mean[ab]**	**R^2**	**Slope (Std. Error)[c]**	**p-Value**
Low	173	104.61	105.03	0.095	0.0119 (0.0073)	0.101
Medium	172	104.71	105.25			
High	173	108.92	107.94			

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED						
Initial Dioxin Category Summary Statistics			**Analysis Results for Log_2 (Initial Dioxin)[d]**			
Initial Dioxin	**n**	**Adj. Mean[ad]**	**R^2**	**Adj. Slope (Std. Error)[c]**	**p-Value**	**Covariate Remarks**
Low	170	110.27**	0.201	0.0248 (0.0083)**	0.003**	INIT*OCC (p=0.013) AGE (p=0.005) RACE (p=0.018) BFAT (p=0.001) OCC*FAMDIAB (p=0.002) PERS*FAMDIAB (p=0.007)
Medium	167	112.56**				
High	168	117.28**				

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Slope and standard error based on natural logarithm of fasting glucose versus log_2 (initial dioxin).

[d] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Log_2 (initial dioxin)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted mean, adjusted slope, standard error, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table N-2-10 for further analysis of this interaction.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 18-24. (Continued)
Analysis of Fasting Glucose (mg/dl) (All Participants)
(Continuous)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED					
Dioxin Category	**n**	**Mean[a]**	**Adj. Mean[ab]**	**Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]**	**p-Value[d]**
Comparison	1,060	104.05	104.02		
Background RH	374	102.35	104.20	0.18 --	0.881
Low RH	258	104.98	103.97	-0.05 --	0.971
High RH	260	107.16	105.58	1.56 --	0.266
Low plus High RH	518	106.06	104.77	0.75 --	0.486

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED					
Dioxin Category	**n**	**Adj. Mean[ae]**	**Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]**	**p-Value[d]**	**Covariate Remarks**
Comparison	1,045	107.43**			DXCAT*OCC (p=0.015) FAMDIAB (p<0.001) AGE*BFAT (p=0.015) RACE*OCC (p<0.001)
Background RH	368	107.14**	-0.29 --**	0.820**	
Low RH	252	106.65**	-0.77 --**	0.588**	
High RH	254	110.16**	2.74 --**	0.067**	
Low plus High RH	506	108.40**	0.97 --**	0.385**	

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Difference of adjusted means after transformation to original scale; confidence interval on difference of adjusted means not given because analysis was performed on natural logarithm scale.

[d] P-value is based on difference of means on natural logarithm scale.

[e] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Categorized dioxin-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted mean, difference of adjusted means, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table N-2-10 for further analysis of this interaction.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤10 ppt.
Background (Ranch Hand): Current Dioxin ≤10 ppt.
Low (Ranch Hand): Current Dioxin >10 ppt, 10 ppt < Initial Dioxin ≤143 ppt.
High (Ranch Hand): Current Dioxin >10 ppt, Initial Dioxin >143 ppt.

Table 18-24. (Continued)
Analysis of Fasting Glucose (mg/dl) (All Participants) (Continuous)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED						
	Current Dioxin Category Mean[a]/(n)			Analysis Results for Log_2 (Current Dioxin + 1)		
Model[b]	Low	Medium	High	R^2	Slope (Std. Error)[c]	p-Value
4	101.39 (295)	105.70 (299)	106.41 (298)	0.018	0.0185 (0.0046)	<0.001
5	101.34 (300)	103.86 (296)	108.43 (296)	0.026	0.0193 (0.0039)	<0.001
6[d]	101.39 (299)	103.86 (296)	108.43 (296)	0.053	0.0116 (0.0042)	0.005

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED							
	Current Dioxin Category Adjusted Mean[a]/(n)			Analysis Results for Log_2 (Current Dioxin + 1)			
Model[b]	Low	Medium	High	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
4	103.01 (290)	105.50 (294)	108.71 (290)	0.102	0.0217 (0.0054)	<0.001	AGE*BFAT (p=0.033) OCC*FAMDIAB (p=0.028) BFAT*FAMDIAB (p=0.045)
5	102.71 (296)**	103.84 (290)**	110.87 (288)**	0.112	0.0214 (0.0046)**	<0.001**	CURR*BFAT (p=0.044) AGE*BFAT (p=0.008) OCC*FAMDIAB (p=0.023) BFAT*FAMDIAB (p=0.034)
6[e]	106.81 (295)	106.64 (290)	110.94 (288)	0.117	0.0122 (0.0044)	0.005	RACE (p=0.075) BFAT (p<0.001) AGE*FAMDIAB (p=0.036)

[a] Transformed from natural logarithm scale.

[b] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[c] Slope and standard error based on natural logarithm of fasting glucose versus log_2 (current dioxin + 1).

[d] Adjusted for log_2 total lipids.

[e] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted mean, adjusted slope, standard error, p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table N-2-10 for further analysis of this interaction.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

body fat-by-family history of diabetes interactions were significant in the Model 4 and 5 analyses. The Model 6 analysis retained race, body fat, and the of age-by-family history of diabetes interaction.

Fasting Glucose (All Participants—Discrete)

For Ranch Hands versus Comparisons, the difference in the percentages of participants with abnormally high fasting glucose was not significant in the Model 1 unadjusted and adjusted analyses (Table 18-25(a,b): p>0.69 for all contrasts). Age, race, occupation, body fat, and the personality type-by-family history of diabetes interaction were significant.

No significant associations between fasting glucose and dioxin were disclosed in the Model 2 and 3 unadjusted and adjusted analyses (Table 18-25(c-f): p>0.28 for all analyses). Covariates retained in the Model 2 adjusted analysis included age, race, body fat, and the personality type-by-family history of diabetes interaction. The Model 3 adjusted analysis retained age, race, and family history of diabetes.

Each of the Model 4 through 6 unadjusted analyses of fasting glucose revealed a significant or marginally significant association with current dioxin. For Model 4, the percentages of Ranch Hands with abnormally high fasting glucose were 8.5 percent, 17.1 percent, and 14.8 percent for the low, medium, and high dioxin categories (Table 18-25(g): p=0.011, Est. RR=1.18). For Models 5 and 6, there were respectively 7.3 percent and 7.4 percent participants with abnormally high fasting glucose in the low dioxin category compared to 16.6 percent for each of the medium and high categories (p=0.001, Est. RR=1.21 for Model 5 and p=0.092, Est. RR=1.11 for Model 6). After adjusting for significant covariates, the association between fasting glucose and current dioxin remained significant for Models 4 and 5 but became nonsignificant for Model 6 (Table 18-25(h): p=0.038, Adj. RR=1.18; p=0.005, Adj. RR=1.22; and p=0.156). However, subsequent analysis removing body fat from the final analysis for Model 6 led to a significant association with current dioxin (Table N-3-12: p=0.010, Adj. RR=1.20). The significant covariates were age, race, body fat, and the personality type-by-family history of diabetes interaction, for Models 4 and 5, and age, race, body fat, and family history of diabetes for Model 6.

Fasting Glucose (Diabetics—Continuous)

Results from the Model 1 unadjusted analysis of fasting glucose on diabetics were not significant (Table 18-26(a): p>0.47 for all contrasts). In the adjusted analysis, a significant interaction between group and age was revealed (Table 18-26(b): p=0.031). Appendix Table N-2-11 displays the results from further investigation of the interaction. Subsequent analysis with the interaction deleted from the final model did not show significant differences in mean fasting glucose between Ranch Hands and Comparisons (p>0.58 for all contrasts). The age-by-occupation, race-by-personality type, race-by-family history of diabetes, occupation-by-diabetic severity, and body fat-by-family history of diabetes were significant in the adjusted analysis.

In the unadjusted Model 2 analysis restricted to diabetics only, a significant association between fasting glucose and initial dioxin was revealed (Table 18-26(c): p=0.031,

Table 18-25.
Analysis of Fasting Glucose (All Participants)
(Discrete)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Percent Abnormal High	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***950***	***13.4***	***1.03 (0.80,1.31)***	***0.891***
	Comparison	***1,277***	***13.1***		
Officer	Ranch Hand	365	13.2	1.06 (0.71,1.58)	0.874
	Comparison	502	12.5		
Enlisted Flyer	Ranch Hand	162	14.2	0.95 (0.53,1.71)	0.979
	Comparison	202	14.9		
Enlisted Groundcrew	Ranch Hand	423	13.2	1.03 (0.71,1.49)	0.956
	Comparison	573	12.9		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks[a]
All	***1.01 (0.78,1.32)***	***0.912***	AGE (p<0.001) RACE (p=0.002) OCC (p=0.082) BFAT (p<0.001) PERS*FAMDIAB (p=0.031)
Officer	1.03 (0.68,1.58)	0.874	
Enlisted Flyer	0.88 (0.47,1.65)	0.693	
Enlisted Groundcrew	1.06 (0.71,1.59)	0.784	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 18-25. (Continued)
Analysis of Fasting Glucose (All Participants)
(Discrete)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Abnormal High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	173	16.8	0.96 (0.80,1.16)	0.690
Medium	172	15.1		
High	173	16.8		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
505	1.03 (0.84,1.27)	0.747	AGE (p<0.001) RACE (p=0.011) BFAT (p=0.113) PERS*FAMDIAB (p=0.003)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 18-25. (Continued)
Analysis of Fasting Glucose (All Participants)
(Discrete)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Percent Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,060	13.0		
Background RH	374	9.6	0.91 (0.61,1.35)	0.628
Low RH	258	17.1	1.23 (0.84,1.82)	0.284
High RH	260	15.4	1.00 (0.67,1.50)	0.983
Low plus High RH	518	16.2	1.12 (0.82,1.52)	0.487

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,045			AGE ($p<0.001$) RACE ($p=0.001$) FAMDIAB ($p=0.007$)
Background RH	368	0.80 (0.53,1.21)	0.281	
Low RH	252	1.09 (0.73,1.62)	0.684	
High RH	254	1.18 (0.78,1.80)	0.430	
Low plus High RH	506	1.13 (0.82,1.56)	0.450	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 18-25. (Continued)
Analysis of Fasting Glucose (All Participants)
(Discrete)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Abnormal High/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	8.5 (295)	17.1 (299)	14.8 (298)	1.18 (1.04,1.34)	0.011
5	7.3 (300)	16.6 (296)	16.6 (296)	1.21 (1.08,1.36)	0.001
6[c]	7.4 (299)	16.6 (296)	16.6 (296)	1.11 (0.98,1.26)	0.092

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	873	1.18 (1.01,1.38)	0.038	AGE ($p<0.001$) RACE ($p=0.019$) BFAT ($p<0.001$) PERS*FAMDIAB ($p=0.037$)
5	873	1.22 (1.06,1.40)	0.005	AGE ($p<0.001$) RACE ($p=0.016$) BFAT ($p<0.001$) PERS*FAMDIAB ($p=0.044$)
6[d]	873	1.11 (0.96,1.29)	0.156	AGE ($p<0.001$) RACE ($p=0.006$) BFAT ($p<0.001$) FAMDIAB ($p=0.041$)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 18-26.
Analysis of Fasting Glucose (mg/dl) (Diabetics) (Continuous)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	*Ranch Hand*	*142*	*140.11*	*-3.43 --*	*0.533*
	Comparison	*179*	*143.54*		
Officer	Ranch Hand	55	141.34	-6.59 --	0.472
	Comparison	58	147.92		
Enlisted Flyer	Ranch Hand	25	141.79	-2.75 --	0.841
	Comparison	36	144.54		
Enlisted Groundcrew	Ranch Hand	62	138.36	-1.85 --	0.820
	Comparison	85	140.21		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Group	n	Adj. Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]	Covariate Remarks[d]
All	*Ranch Hand*	*137*	*156.94***	*-2.85 --***	0.613**	GROUP*AGE (p=0.031)
	Comparison	*177*	*159.79***			AGE*OCC (p=0.009)
Officer	Ranch Hand	53	165.33**	-5.49 --**	0.589**	RACE*PERS (p=0.039)
	Comparison	58	170.82**			RACE*FAMDIAB (p=0.027)
Enlisted Flyer	Ranch Hand	24	153.01**	-3.68 --**	0.781**	OCC*DIABSEV (p<0.001)
	Comparison	34	156.69**			BFAT*FAMDIAB (p=0.001)
Enlisted Groundcrew	Ranch Hand	60	152.28**	-0.74 --**	0.926**	
	Comparison	85	153.02**			

[a] Transformed from the natural logarithm scale.

[b] Difference of means after transformation to original scale; confidence interval on difference of means not given because analysis was performed on natural logarithm scale.

[c] P-values based on difference of means on natural logarithm scale.

[d] Covariates and associated p-values correspond to final model based on all participants with available data.

** Group-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted mean, difference of adjusted means, confidence interval and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table N-2-11 for further analysis of this interaction.

Table 18-26. (Continued)
Analysis of Fasting Glucose (mg/dl) (Diabetics)
(Continuous)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	31	130.76	132.71	0.134	0.0529 (0.0242)	0.031
Medium	31	138.17	139.80			
High	34	164.76	160.82			

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED						
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[d]			
Initial Dioxin	n	Adj. Mean[ad]	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
Low	31	157.21	0.343	0.0431 (0.0225)	0.059	RACE (p=0.087) BFAT (p=0.020) DIABSEV (p=0.005)
Medium	31	162.82				
High	34	184.05				

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Slope and standard error based on natural logarithm of fasting glucose versus log_2 (initial dioxin).

[d] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 18-26. (Continued)
Analysis of Fasting Glucose (mg/dl) (Diabetics)
(Continuous)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED					
Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	148	142.19	141.80		
Background RH	42	131.44	135.64	-6.16 --	0.463
Low RH	49	132.99	132.19	-9.62 --	0.210
High RH	47	157.47	155.41	13.61 --	0.108
Low plus High RH	96	144.46	143.09	1.28 --	0.838

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED					
Dioxin Category	n	Adj. Mean[ae]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]	Covariate Remarks
Comparison	147	159.30			AGE*OCC (p<0.001) AGE*DIABSEV (p=0.025) RACE*PERS (p=0.026) OCC*DIABSEV (p<0.001) BFAT*FAMDIAB (p=0.023)
Background RH	39	161.35	2.05 --	0.825	
Low RH	48	146.68	-12.62 --	0.112	
High RH	46	168.57	9.26 --	0.289	
Low plus High RH	94	157.01	-2.29 --	0.718	

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Difference of adjusted means after transformation to original scale; confidence interval on difference of adjusted means not given because analysis was performed on natural logarithm scale.

[d] P-value is based on difference of means on natural logarithm scale.

[e] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 18-26. (Continued)
Analysis of Fasting Glucose (mg/dl) (Diabetics)
(Continuous)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED						
	Current Dioxin Category Mean[a]/(n)			Analysis Results for Log_2 (Current Dioxin + 1)		
Model[b]	Low	Medium	High	R^2	Slope (Std. Error)[c]	p-Value
4	128.30 (28)	135.91 (56)	152.07 (54)	0.072	0.0603 (0.0185)	0.001
5	131.30 (26)	124.92 (54)	161.22 (58)	0.089	0.0558 (0.0153)	<0.001
6[d]	137.72 (26)	126.76 (54)	155.67 (58)	0.117	0.0389 (0.0172)	0.025

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED							
	Current Dioxin Category Adjusted Mean[a]/(n)			Analysis Results for Log_2 (Current Dioxin + 1)			
Model[b]	Low	Medium	High	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
4	161.99 (26)	160.48 (55)	178.30 (52)	0.400	0.0442 (0.0219)	0.046	RACE (p=0.128) BFAT (p=0.068) OCC*DIABSEV (p=0.010) FAMDIAB*DIABSEV (p=0.020)
5	169.50 (24)	149.54 (53)	189.42 (56)	0.408	0.0429 (0.0177)	0.017	RACE (p=0.116) BFAT (p=0.095) OCC*DIABSEV (p=0.015) FAMDIAB*DIABSEV (p=0.024)
6[e]	174.95 (24)	151.27 (53)	184.18 (56)	0.421	0.0266 (0.0204)	0.195	RACE (p=0.112) BFAT (p=0.099) OCC*DIABSEV (p=0.015) FAMDIAB*DIABSEV (p=0.028)

[a] Transformed from natural logarithm scale.

[b] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[c] Slope and standard error based on natural logarithm of fasting glucose versus log_2 (current dioxin + 1).

[d] Adjusted for log_2 total lipids.

[e] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Slope=0.0529). With adjustment for percent body fat at the time of duty in SEA, and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, mean fasting glucose levels were 132.71 mg/dl and 139.80 mg/dl for the low and medium initial dioxin categories in contrast to 160.82 mg/dl for the high category. After adjusting for race, body fat, and diabetic severity, the dioxin effect remained significant (Table 18-26(d): p=0.059, Slope=0.0431). The adjusted fasting glucose level was again greater for the high dioxin category (184.05 mg/dl) than for the low and medium categories (157.21 mg/dl and 162.82 mg/dl).

No statistically significant differences in mean fasting glucose between the Ranch Hand dioxin categories and the Comparison group were evident from either the unadjusted or adjusted Model 3 analyses (Table 18-26(e,f): p>0.10 for all contrasts). The age-by-occupation, age-by-diabetic severity, race-by-personality type, occupation-by-diabetic severity, and body fat-by family history of diabetes interactions were significant in the adjusted analysis.

Significant positive associations between current dioxin and fasting glucose in diabetics were seen in each of the unadjusted Model 4 through 6 analyses. For Model 4, average fasting glucose levels for the low, medium, and high dioxin categories were 128.30 mg/dl, 135.91 mg/dl, and 152.07 mg/dl respectively (Table 18-26(g): p=0.001, Slope=0.0603). For Model 5, the respective means for fasting glucose were 131.30 mg/dl, 124.92 mg/dl, and 161.22 mg/dl (p<0.001, Slope=0.0558) and for Model 6, the respective means were 137.72 mg/dl, 126.76 mg/dl, and 155.67 mg/dl (p=0.025, Slope=0.0389).

In the adjusted analyses, the current dioxin effect remained significant for Models 4 and 5 but became nonsignificant for Model 6 (Table 18-26(h): p=0.046, Slope=0.0442 for Model 4; p=0.017, Slope=0.0429 for Model 5; and p=0.195, Slope=0.0266 for Model 6). For Model 4, the adjusted means were 161.99 mg/dl for the low dioxin category and 160.48 mg/dl for the medium category in comparison to 178.30 mg/dl for the high category. A similar pattern was seen in the adjusted means for Model 5 with an average fasting glucose level of 169.50 mg/dl in the low category, 149.54 mg/dl in the medium category, and 189.42 mg/dl in the high category. For Models 4, 5, and 6, race, body fat, and the occupation-by-diabetic severity and family history of diabetes-by-diabetic severity interactions were retained. For Model 6, removal of occupation and body fat from the final model led to a marginally significant association between fasting glucose in diabetics and current dioxin (Appendix Table N-3-13: p=0.057, Slope=0.0345). For the low, medium, and high categories of initial dioxin, the adjusted mean fasting glucose was 160.14 mg/dl, 150.27 mg/dl, and 175.97 mg/dl respectively. The association between fasting glucose in diabetics and current dioxin remained significant in Models 4 and 5 after removing occupation and body fat from the final model.

Fasting Glucose (Diabetics—Discrete)

In the Model 1 analyses of discrete fasting glucose restricted to diabetics, no significant differences between Ranch Hands and Comparisons were disclosed (Table 18-27(a,b): p>0.61 for the unadjusted and adjusted analyses). Age, race, body fat, and diabetic severity were significant in the adjusted analysis.

Table 18-27.
Analysis of Fasting Glucose (Diabetics)
(Discrete)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Abnormal High**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	*Ranch Hand*	*142*	*69.0*	*0.99 (0.61,1.59)*	*0.999*
	Comparison	*179*	*69.3*		
Officer	Ranch Hand	55	69.1	0.78 (0.34,1.77)	0.699
	Comparison	58	74.1		
Enlisted Flyer	Ranch Hand	25	76.0	1.58 (0.50,5.00)	0.617
	Comparison	36	66.7		
Enlisted Groundcrew	Ranch Hand	62	66.1	0.96 (0.48,1.92)	0.999
	Comparison	85	67.1		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	*0.96 (0.58,1.60)*	*0.878*	AGE (p=0.003) RACE (p=0.048) BFAT (p=0.006) DIABSEV (p=0.001)
Officer	0.87 (0.37,2.05)	0.745	
Enlisted Flyer	1.29 (0.38,4.33)	0.682	
Enlisted Groundcrew	0.94 (0.45,1.97)	0.867	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 18-27. (Continued)
Analysis of Fasting Glucose (Diabetics)
(Discrete)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Abnormal High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	31	64.5	0.96 (0.69,1.34)	0.830
Medium	31	77.4		
High	34	70.6		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
96	0.89 (0.61,1.28)	0.518	BFAT (p=0.093) DIABSEV (p=0.001)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 18-27. (Continued)
Analysis of Fasting Glucose (Diabetics)
(Discrete)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	**n**	**Percent Abnormal High**	**Est. Relative Risk (95% C.I.)[ab]**	**p-Value**
Comparison	148	68.2		
Background RH	42	64.3	1.11 (0.52,2.37)	0.778
Low RH	49	69.4	1.04 (0.51,2.13)	0.908
High RH	47	72.3	1.15 (0.55,2.41)	0.716
Low plus High RH	96	70.8	1.09 (0.62,1.94)	0.762

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	**n**	**Adj. Relative Risk (95% C.I.)[ac]**	**p-Value**	**Covariate Remarks**
Comparison	147			DXCAT*BFAT (p=0.018) AGE (p=0.040) RACE (p=0.008) FAMDIAB (p=0.149) DIABSEV (p<0.001)
Background RH	39	1.08 (0.48,2.46)**	0.847**	
Low RH	48	0.82 (0.38,1.77)**	0.615**	
High RH	46	1.07 (0.47,2.43)**	0.871**	
Low plus High RH	94	0.93 (0.50,1.72)**	0.813**	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Categorized dioxin-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table N-2-12 for further analysis of this interaction.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 18-27. (Continued)
Analysis of Fasting Glucose (Diabetics)
(Discrete)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Abnormal High/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	64.3 (28)	69.6 (56)	70.4 (54)	1.13 (0.89,1.44)	0.316
5	57.7 (26)	68.5 (54)	74.1 (58)	1.15 (0.94,1.41)	0.172
6[c]	57.7 (26)	68.5 (54)	74.1 (58)	1.05 (0.83,1.32)	0.701

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	138	****	****	CURR*BFAT ($p<0.001$) DIABSEV ($p<0.001$)
5	138	****	****	CURR*BFAT ($p<0.001$) DIABSEV ($p<0.001$)
6[d]	138	****	****	CURR*BFAT ($p<0.001$) DIABSEV ($p<0.001$)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

**** Log_2 (current dioxin + 1)-by-covariate interaction ($p \leq 0.01$); adjusted relative risk, confidence interval, and p-value not presented; refer to Appendix Table N-2-12 for further analysis of this interaction.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

The Model 2 and 3 unadjusted analyses did not reveal any significant associations between fasting glucose in diabetics and dioxin (Table 18-27(c,e): p>0.71 for all analyses). Adjustment for body fat and diabetic severity in Model 2 did not reveal a significant relationship between fasting glucose and initial dioxin (Table 18-27(d): p=0.518).

In the Model 3 adjusted analysis of discrete fasting glucose in diabetics, the interaction of categorized dioxin and body fat was significant (Table 18-27(f): p=0.018). Appendix Table N-2-12 presents the results stratified by body fat (obese; lean or normal). Removing the interaction from the final model did not reveal any significant differences between the four Ranch Hand categories and the Comparisons group (p>0.61 for all contrasts). Age, race, family history of diabetes, and diabetic severity were significant covariates.

For Models 4 through 6, the unadjusted analyses did not detect a significant association between fasting glucose in diabetes and current dioxin (Table 18-27(g): p>0.17). However, in each of the adjusted analyses, the interaction of current dioxin and body fat was highly significant (Table 18-27(h): p<0.001 for all interactions). The stratified results from analyses on these interactions are found in Appendix Table N-2-12 but do not reveal any significant associations between fasting glucose in diabetics and current dioxin. Diabetic severity was an additional covariate retained in each of the adjusted analyses.

Fasting Glucose (Nondiabetics—Continuous)

In the Model 1 unadjusted analysis of fasting glucose restricted to nondiabetics, no overall significant difference between Ranch Hands and Comparisons was found to exist (Table 18-28(a): p=0.925). However, the stratified analyses within the three levels of occupation revealed a significant difference between the two groups in the enlisted flyer category (p=0.015, Diff. of Means=-2.52). For this category, the fasting glucose mean for the Ranch Hands was 98.22 mg/dl and 100.75 mg/dl for the Comparisons. In the adjusted analysis, a significant interaction between group and occupation was revealed (Table 18-28(b): p=0.024). The difference between Ranch Hands and Comparisons in the enlisted flyer category was significant (p=0.012, Diff of Adj. Means=-2.45). For Ranch Hands, the adjusted mean fasting glucose level was 98.01 mg/dl compared to 100.46 mg/dl for Comparisons. The remaining contrasts between Ranch Hands and Comparisons were positive but not significant. After removing the interaction from the final model, the overall contrast between Ranch Hands and Comparisons was nonsignificant (p=0.957). Personality, body fat, and the age-by-family history of diabetes interaction were significant.

Neither of the unadjusted analyses for Models 2 and 3 revealed a significant association between fasting glucose in nondiabetics and dioxin (Table 18-28(c,e): p>0.18 for all analyses). The adjusted Model 2 analysis revealed a significant interaction between initial dioxin and occupation (Table 18-28: p=0.010). Appendix Table N-2-13 contains additional information regarding this interaction. No significant results were evident after the interaction was removed from the final model (p=0.880). The age-by-occupation, age-by-body fat, and personality type-by-family history of diabetes interactions were significant covariates in the adjusted model.

Table 18-28.
Analysis of Fasting Glucose (mg/dl) (Nondiabetics)
(Continuous)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	*Ranch Hand*	*808*	*99.02*	*-0.04 --*	*0.925*
	Comparison	*1,098*	*99.06*		
Officer	Ranch Hand	310	99.75	0.42 --	0.491
	Comparison	444	99.33		
Enlisted Flyer	Ranch Hand	137	98.22	-2.52 --	0.015
	Comparison	166	100.75		
Enlisted Groundcrew	Ranch Hand	361	98.70	0.46 --	0.451
	Comparison	488	98.24		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Group	n	Adj. Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]	Covariate Remarks[d]
All	*Ranch Hand*	*794*	*99.18***	*-0.02 -- ***	0.957**	GROUP*OCC (p=0.024)
	Comparison	*1,081*	*99.20***			PERS (p=0.144)
Officer	Ranch Hand	306	99.27	0.40 --	0.523	BFAT (p<0.001)
	Comparison	441	98.88			AGE*FAMDIAB (p=0.030)
Enlisted Flyer	Ranch Hand	134	98.01	-2.45 --	0.012	
	Comparison	163	100.46			
Enlisted Groundcrew	Ranch Hand	354	99.45	0.49 --	0.400	
	Comparison	477	98.95			

[a] Transformed from the natural logarithm scale.

[b] Difference of means after transformation to original scale; confidence interval on difference of means not given because analysis was performed on natural logarithm scale.

[c] P-values based on difference of means on natural logarithm scale.

[d] Covariates and associated p-values correspond to final model based on all participants with available data.

** Group-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted mean, difference of adjusted means, confidence interval and p-value derived from a model fitted after deletion of this interaction.

Table 18-28. (Continued)
Analysis of Fasting Glucose (mg/dl) (Nondiabetics)
(Continuous)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	142	99.64	99.70	0.024	-0.0035 (0.0033)	0.290
Medium	141	98.52	98.61			
High	139	98.43	98.28			

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED						
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[d]			
Initial Dioxin	n	Adj. Mean[ad]	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
Low	139	100.20**	0.115	0.0006 (0.0038)**	0.880**	INIT*OCC (p=0.010) AGE*OCC (p=0.024) AGE*BFAT (p=0.026) PERS*FAMDIAB (p=0.027)
Medium	137	99.92**				
High	135	100.22**				

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Slope and standard error based on natural logarithm of fasting glucose versus $\log_2$ (initial dioxin).

[d] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Log_2 (initial dioxin)-by-covariate interaction ($p \leq 0.05$); adjusted mean, adjusted slope, standard error, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table N-2-13 for further analysis of this interaction.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 18-28. (Continued)
Analysis of Fasting Glucose (mg/dl) (Nondiabetics)
(Continuous)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	912	98.91	98.91		
Background RH	332	99.16	99.56	0.66 --	0.235
Low RH	209	99.31	99.11	0.21 --	0.752
High RH	213	98.43	98.03	-0.87 --	0.180
Low plus High RH	422	98.87	98.57	-0.34 --	0.507

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Mean[ae]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]	Covariate Remarks
Comparison	897	****			DXCAT*OCC (p=0.004) PERS (p=0.133) BFAT (p<0.001) AGE*OCC (p=0.016) AGE*FAMDIAB (p=0.018)
Background RH	329	****	****	****	
Low RH	203	****	****	****	
High RH	208	****	****	****	
Low plus High RH	411	****	****	****	

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Difference of adjusted means after transformation to original scale; confidence interval on difference of adjusted means not given because analysis was performed on natural logarithm scale.

[d] P-value is based on difference of means on natural logarithm scale.

[e] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

**** Categorized dioxin-by-covariate interaction ($p \leq 0.01$); adjusted mean, difference of adjusted means, confidence interval, and p-value not given; refer to Appendix Table N-2-13 for further analysis of this interaction.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 18-28. (Continued)
Analysis of Fasting Glucose (mg/dl) (Nondiabetics)
(Continuous)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED						
	Current Dioxin Category Mean[a]/(n)			Analysis Results for Log_2 (Current Dioxin + 1)		
Model[b]	Low	Medium	High	R^2	Slope (Std. Error)[c]	p-Value
4	98.92 (267)	99.75 (243)	98.33 (244)	<0.001	-0.0002 (0.0022)	0.943
5	99.88 (274)	99.67 (242)	98.45 (238)	<0.001	0.0009 (0.0019)	0.650
6[d]	99.20 (273)	99.67 (242)	98.14 (238)	0.006	-0.0009 (0.0020)	0.656

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED							
	Current Dioxin Category Adjusted Mean[a]/(n)			Analysis Results for Log_2 (Current Dioxin + 1)			
Model[b]	Low	Medium	High	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
4	99.45 (264)	99.71 (238)	99.04 (238)	0.083	0.0001 (0.0026)	0.975	PERS (p=0.094) AGE*OCC (p=0.015) AGE*BFAT (p=0.001) AGE*FAMDIAB (p=0.004) OCC*FAMDIAB (p=0.027)
5	99.32 (272)	99.89 (236)	99.02 (232)	0.083	0.0009 (0.0022)	0.688	PERS (p=0.100) AGE*OCC (p=0.013) AGE*BFAT (p=0.001) AGE*FAMDIAB (p=0.004) OCC*FAMDIAB (p=0.027)
6[e]	99.34 (273)	99.36 (241)	98.14 (238)	0.057	-0.0014 (0.0021)	0.510	PERS (p=0.117) AGE*BFAT (p=0.008)

[a] Transformed from natural logarithm scale.

[b] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[c] Slope and standard error based on natural logarithm of fasting glucose versus log_2 (current dioxin + 1).

[d] Adjusted for log_2 total lipids.

[e] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤46 ppq; Medium = >46-128 ppq; High = >128 ppq.

For Model 3, the adjusted analysis of fasting glucose in nondiabetics disclosed a highly significant interaction between categorized dioxin and occupation (Table 18-28(f): p=0.004). This interaction is further examined in Appendix Table N-2-13. Personality type, body fat, and the age-by-occupation and age-by-family history of diabetes interactions were significant in the Model 3 analysis. After removing the categorized dioxin-by-occupation interaction and body fat and occupation from the final model, no significant differences were found between the four Ranch Hand categories and the Comparison group (Appendix Table N-3-15: p>0.46).

No significant associations between fasting glucose in nondiabetics and current dioxin were evident from either the unadjusted or adjusted analyses of Models 4 through 6 (Table 18-28: p>0.51 for all analyses). Personality type and the age-by-occupation, age-by-body fat, age-by-family history of diabetes, and occupation-by-family history of diabetes interactions were retained in the adjusted analyses of Models 4 and 5. For Model 6, significant covariates included personality type and the age-by-body fat interaction.

Fasting Glucose (Nondiabetics—Discrete)

Overall and occupationally stratified differences between Ranch Hands and Comparisons were nonsignificant in both the unadjusted and adjusted Model 1 analyses of fasting glucose in its discrete form restricted to nondiabetics (Table 18-29(a,b): p>0.37 for all contrasts). Age and body fat were retained in the adjusted analysis.

The unadjusted and adjusted analysis for Models 2 and 3, investigating the relationship between fasting glucose and dioxin in nondiabetics were nonsignificant (Table 18-29(c-f): p>0.15 for all analyses). The Model 2 adjusted analyses retained race and family history of diabetes, while Model 3 retained the occupation-by-family history of diabetes and the occupation-by-age interactions.

Current dioxin was not significantly associated with discrete fasting glucose for nondiabetics in the unadjusted and adjusted analyses of Models 4 through 6 (Table 18-29(g,h): p>0.43 for all analyses). Body fat was significant in each of the adjusted analyses. Additionally, race was retained in the Model 6 analysis.

2-Hour Postprandial Glucose (Continuous)

In the Model 1 unadjusted analysis of 2-hour postprandial glucose on nondiabetics, no significant group effect was revealed (Table 18-30(a): p>0.21 for all contrasts). However, in the adjusted analysis, highly significant interactions between group and body fat and between group and family history of diabetes were revealed (Table 18-30(b): p=0.001 and p=0.009 respectively). Results from additional analyses on these interactions are found in Appendix Table N-2-14. Additionally, age and the occupation-by-personality type interaction were retained in the adjusted analysis.

The unadjusted Model 2 and 3 analyses of 2-hour postprandial glucose in nondiabetics did not reveal a significant positive dioxin effect (Table 18-30(c,e): p>0.32 for all analyses). However, in Model 2, adjustment for age, personality type, and body fat led to a significant positive association between initial dioxin and 2-hour postprandial glucose (Table 18-30(d):

Table 18-29.
Analysis of Fasting Glucose (Nondiabetics)
(Discrete)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Abnormal High**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***808***	***3.6***	***0.91 (0.57,1.48)***	***0.804***
	Comparison	***1,098***	***3.9***		
Officer	Ranch Hand	310	3.2	0.71 (0.33,1.53)	0.487
	Comparison	444	4.5		
Enlisted Flyer	Ranch Hand	137	2.9	0.80 (0.22,2.90)	0.989
	Comparison	166	3.6		
Enlisted Groundcrew	Ranch Hand	361	4.2	1.20 (0.59,2.44)	0.745
	Comparison	488	3.5		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***0.92 (0.57,1.48)***	***0.719***	AGE (p=0.004) BFAT (p<0.001)
Officer	0.70 (0.32,1.53)	0.371	
Enlisted Flyer	0.75 (0.21,2.74)	0.665	
Enlisted Groundcrew	1.25 (0.61,2.56)	0.542	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 18-29. (Continued)
Analysis of Fasting Glucose (Nondiabetics)
(Discrete)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Abnormal High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	142	6.3	0.83 (0.55,1.26)	0.372
Medium	141	1.4		
High	139	3.6		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
412	0.73 (0.46,1.15)	0.153	RACE (p=0.075) FAMDIAB (p=0.094)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 18-29. (Continued)
Analysis of Fasting Glucose (Nondiabetics)
(Discrete)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Abnormal High	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	912	4.1		
Background RH	332	2.7	0.73 (0.35,1.53)	0.401
Low RH	209	4.8	1.13 (0.55,2.31)	0.745
High RH	213	2.8	0.63 (0.26,1.51)	0.297
Low plus High RH	422	3.8	0.87 (0.48,1.58)	0.644

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	898			OCC*FAMDIAB (p=0.028) OCC*AGE (p=0.043)
Background RH	329	0.71 (0.33,1.52)	0.373	
Low RH	204	1.15 (0.56,2.39)	0.705	
High RH	208	0.58 (0.22,1.56)	0.284	
Low plus High RH	412	0.88 (0.47,1.66)	0.701	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 18-29. (Continued)
Analysis of Fasting Glucose (Nondiabetics)
(Discrete)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Abnormal High/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	2.6 (267)	4.9 (243)	2.5 (244)	1.02 (0.77,1.34)	0.907
5	2.6 (274)	5.0 (242)	2.5 (238)	1.05 (0.82,1.33)	0.714
6[c]	2.6 (273)	5.0 (242)	2.5 (238)	0.99 (0.76,1.28)	0.920

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	754	0.92 (0.68,1.24)	0.583	BFAT (p=0.022)
5	754	0.96 (0.75,1.24)	0.772	BFAT (p=0.027)
6[d]	753	0.90 (0.68,1.18)	0.439	BFAT (p=0.021) RACE (p=0.121)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 18-30.
Analysis of 2-Hour Postprandial Glucose (mg/dl) (Nondiabetics) (Continuous)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Mean[a]**	**Difference of Means (95% C.I.)[b]**	**p-Value[c]**
All	*Ranch Hand*	*807*	*103.90*	*0.63 --*	*0.630*
	Comparison	*1,097*	*103.27*		
Officer	Ranch Hand	310	103.61	2.43 --	0.219
	Comparison	444	101.18		
Enlisted Flyer	Ranch Hand	137	106.60	-1.94 --	0.554
	Comparison	166	108.54		
Enlisted Groundcrew	Ranch Hand	360	103.14	-0.30 --	0.884
	Comparison	487	103.44		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED						
Occupational Category	**Group**	**n**	**Adj. Mean[a]**	**Difference of Adj. Means (95% C.I.)[b]**	**p-Value[c]**	**Covariate Remarks[d]**
All	*Ranch Hand*	*793*	****	****	****	GROUP*BFAT (p=0.001)
	Comparison	*1,080*				GROUP*FAMDIAB (p=0.009)
Officer	Ranch Hand	306	****	****	****	AGE (p<0.001)
	Comparison	441				OCC*PERS (p=0.012)
Enlisted Flyer	Ranch Hand	134	****	****	****	
	Comparison	163				
Enlisted Groundcrew	Ranch Hand	353	****	****	****	
	Comparison	476				

[a] Transformed from the natural logarithm scale.

[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.

[c] P-values based on difference of means on natural logarithm scale.

[d] Covariates and associated p-values correspond to final model based on all participants with available data.

**** Group-by-covariate interactions ($p \leq 0.01$); adjusted mean, difference of adjusted means, and p-value not presented; refer to Appendix Table N-2-14 for further analysis of these interactions.

Table 18-30. (Continued)
Analysis of 2-Hour Postprandial Glucose (mg/dl) (Nondiabetics) (Continuous)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	142	103.75	104.44	0.067	0.0078 (0.0107)	0.464
Medium	141	106.75	107.35			
High	139	107.84	106.51			

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED						
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[d]			
Initial Dioxin	n	Adj. Mean[ad]	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
Low	141	101.10	0.162	0.0216 (0.0106)	0.041	AGE ($p<0.001$) PERS ($p=0.043$) BFAT ($p<0.001$)
Medium	141	106.99				
High	139	108.72				

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Slope and standard error based on natural logarithm of 2-hour postprandial glucose versus log_2 (initial dioxin).

[d] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 18-30. (Continued)
Analysis of 2-Hour Postprandial Glucose (mg/dl) (Nondiabetics)
(Continuous)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED					
Dioxin Category	**n**	**Mean[a]**	**Adj. Mean[ab]**	**Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]**	**p-Value[d]**
Comparison	911	103.08	103.05		
Background RH	331	100.37	102.28	-0.77 --	0.657
Low RH	209	104.87	104.05	1.00 --	0.633
High RH	213	107.29	105.13	2.07 --	0.322
Low plus High RH	422	106.08	104.59	1.54 --	0.340

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED					
Dioxin Category	**n**	**Adj. Mean[ae]**	**Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]**	**p-Value[d]**	**Covariate Remarks**
Comparison	896	104.72**			DXCAT*BFAT (p<0.001) DXCAT*FAMDIAB (p=0.016) AGE (p<0.001) OCC*PERS (p=0.031)
Background RH	328	104.03**	-0.70 -- **	0.689**	
Low RH	203	105.13**	0.40 -- **	0.845**	
High RH	208	108.06**	3.34 -- **	0.119**	
Low plus High RH	411	106.60**	1.88 -- **	0.245**	

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Difference of adjusted means after transformation to original scale; confidence interval on difference of adjusted means not presented because analysis was performed on natural logarithm scale.

[d] P-value is based on difference of means on natural logarithm scale.

[e] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Categorized dioxin-by-covariate interactions ($p \leq 0.05$); adjusted mean, difference of adjusted means, and p-value derived from a model fitted after deletion of these interactions; refer to Appendix Table N-2-14 for further analysis of these interactions.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 18-30. (Continued)
Analysis of 2-Hour Postprandial Glucose (mg/dl) (Nondiabetics) (Continuous)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

	Current Dioxin Category Mean[a]/(n)			Analysis Results for Log_2 (Current Dioxin + 1)		
Model[b]	Low	Medium	High	R^2	Slope (Std. Error)[c]	p-Value
4	99.88 (266)	103.67 (243)	107.53 (244)	0.018	0.0267 (0.0071)	<0.001
5	99.00 (273)	104.18 (242)	108.31 (238)	0.026	0.0275 (0.0061)	<0.001
6[d]	100.25 (272)	104.17 (242)	106.86 (238)	0.037	0.0214 (0.0065)	0.001

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

	Current Dioxin Category Adjusted Mean[a]/(n)			Analysis Results for Log_2 (Current Dioxin + 1)			
Model[b]	Low	Medium	High	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
4	101.82 (266)	101.15 (242)	107.19 (244)	0.170	0.0177 (0.0071)	0.012	AGE (p<0.001) BFAT (p<0.001) PERS (p=0.138)
5	100.73 (273)	102.19 (241)	107.52 (238)	0.174	0.0189 (0.0061)	0.002	AGE (p<0.001) BFAT (p<0.001) PERS (p=0.141)
6[e]	101.78 (272)	102.24 (241)	106.21 (238)	0.182	0.0134 (0.0064)	0.038	AGE (p<0.001) BFAT (p<0.001) PERS (p=0.090)

[a] Transformed from natural logarithm scale.

[b] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[c] Slope and standard error based on natural logarithm of 2-hour postprandial glucose versus log_2 (current dioxin + 1).

[d] Adjusted for log_2 total lipids.

[e] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

p=0.041, Adj. Slope=0.0216). The 2-hour postprandial glucose adjusted means for the low, medium, and high initial dioxin levels were 101.10 mg/dl, 106.99 mg/dl, and 108.72 mg/dl respectively.

For the Model 3 adjusted analysis of 2-hour postprandial glucose in nondiabetics, interactions between categorized dioxin and body fat and between categorized dioxin and family history of diabetes were revealed (Table 18-30(f): p<0.001 and p=0.016 respectively). Appendix Table N-2-14 contains further information on these interactions. Followup analyses with the interactions removed from the final model did not reveal any significant differences between the four Ranch Hand categories and the Comparison group (Table 18-30(f): p>0.11 for all contrasts). However, when the interactions of body fat, and occupation were removed from the final model, the difference between the high Ranch Hand category and the Comparison group was significant (Table N-3-17: p=0.032, Diff. of Adj. Means = 4.54). Age and the occupation-by-personality type interaction were additional covariates retained in the Model 3 analysis.

Each of the Model 4 through 6 unadjusted analyses revealed a highly significant relationship between current dioxin and 2-hour postprandial glucose in nondiabetics (Table 18-30(g): p<0.001, Slope=0.0267 for Model 4, p<0.001, Slope=0.0275 for Model 5; and p=0.001, Slope=0.0214 for Model 6). The mean levels of 2-hour postprandial glucose for the low, medium, and high categories of lipid-adjusted current dioxin were 99.88 mg/dl, 103.67 mg/dl, and 107.53 mg/dl. For the whole weight-current dioxin categories, mean levels were 99.00 mg/dl, 104.18 mg/dl, and 108.31 mg/dl. For whole-weight current dioxin adjusted for total lipids, mean levels were 100.25 mg/dl, 104.17 mg/dl, and 106.86 mg/dl. The association between current dioxin and 2-hour postprandial glucose remained significant after adjustment for age, body fat, and personality type (Table 18-30(h): p=0.012, Adj. Slope=0.0177 for Model 4, p=0.002, Adj. Slope=0.0189 for Model 5; and p=0.038, Adj. Slope=0.0134 for Model 6). The adjusted mean levels of 2-hour postprandial glucose for low, medium, and high categories of current dioxin were 101.82 mg/dl, 101.15 mg/dl, 107.19 mg/dl for Model 4, 100.73 mg/dl, 102.19 mg/dl, 107.52 mg/dl for Model 5, and 101.78 mg/dl, 102.24 mg/dl, 106.21 mg/dl for Model 6.

2-Hour Postprandial Glucose (Discrete)

A marginally significant difference in the percentage of nondiabetics with impaired 2-hour postprandial glucose levels between Ranch Hands and Comparisons was evident from the overall contrast in the Model 1 unadjusted analysis (Table 18-31(a): p=0.097, Est. RR=1.26). This difference was not apparent, however, from analyses within each of the levels of occupation (p>0.11 for all contrasts). In the adjusted analysis, there was a significant interaction between group and body fat (Table 18-31(b): p=0.042). Results from further analysis on this interaction are presented in Appendix Table N-2-15. A marginally significant difference between Ranch Hands and Comparisons was found for obese nondiabetic participants (Appendix Table N-2-15: p=0.064, Adj. RR=1.56), but the difference was nonsignificant for lean or normal participants (p=0.536). After the interaction was deleted from the final model, a marginally significant difference between Ranch Hands and Comparisons in the enlisted groundcrew category was evident (p=0.064, Adj. RR=1.48). The overall contrast and the remaining occupational contrasts were nonsignificant (p>0.11). Age,

Table 18-31.
Analysis of 2-Hour Postprandial Glucose (Nondiabetics) (Discrete)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Impaired**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***807***	***14.7***	***1.26 (0.97,1.65)***	***0.097***
	Comparison	***1,097***	***12.0***		
Officer	Ranch Hand	310	12.6	1.28 (0.81,2.01)	0.351
	Comparison	444	10.1		
Enlisted Flyer	Ranch Hand	137	15.3	0.93 (0.59,1.73)	0.949
	Comparison	166	16.3		
Enlisted Groundcrew	Ranch Hand	360	16.4	1.39 (0.95,2.06)	0.113
	Comparison	487	12.3		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***1.26 (0.95,1.68)*****	***0.115*****	GROUP*BFAT (p=0.042) OCC*RACE (p=0.017) AGE (p<0.001) PERS (p=0.030) FAMDIAB (p=0.047)
Officer	1.30 (0.81,2.10)**	0.274**	
Enlisted Flyer	0.80 (0.42,1.55)**	0.514**	
Enlisted Groundcrew	1.48 (0.98,2.25)**	0.064**	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

** Group-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table N-2-15 for further analysis of this interaction.

Table 18-31. (Continued)
Analysis of 2-Hour Postprandial Glucose (Nondiabetics)
(Discrete)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Impaired	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	142	15.5	1.09 (0.90,1.33)	0.390
Medium	141	17.0		
High	139	20.1		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
421	1.19 (0.96,1.47)**	0.112**	INIT*RACE (p=0.008) AGE (p=0.001) BFAT (p=0.003) PERS (p=0.122)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

**Log_2 (initial dioxin)-by-covariate interaction ($p \leq 0.05$); adjusted relative risk, confidence interval and p-value derived from a model fitted after deletion of this interaction; refer to Appendix N-2-15 for further analysis of this interaction.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 18-31. (Continued)
Analysis of 2-Hour Postprandial Glucose (Nondiabetics)
(Discrete)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Percent Impaired	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	911	12.0		
Background RH	331	10.0	0.94 (0.62,1.43)	0.765
Low RH	209	15.8	1.30 (0.85,2.00)	0.229
High RH	213	19.2	1.56 (1.04,2.33)	0.031
Low plus High RH	422	17.5	1.43 (1.03,1.99)	0.031

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	896			AGE ($p<0.001$) PERS ($p=0.029$) BFAT ($p<0.001$) RACE*FAMDIAB ($p=0.024$) OCC*RACE ($p=0.009$)
Background RH	328	0.99 (0.63,1.54)	0.961	
Low RH	203	1.24 (0.79,1.96)	0.352	
High RH	208	1.67 (1.07,2.59)	0.023	
Low plus High RH	411	1.44 (1.02,2.04)	0.040	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 18-31. (Continued)
Analysis of 2-Hour Postprandial Glucose (Nondiabetics) (Discrete)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Impaired/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	10.2 (266)	13.2 (243)	19.7 (244)	1.27 (1.11,1.46)	0.001
5	8.4 (273)	14.5 (242)	20.6 (238)	1.28 (1.13,1.45)	<0.001
6[c]	8.5 (272)	14.5 (242)	20.6 (238)	1.23 (1.08,1.41)	0.002

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	753	1.27 (1.08,1.50)**	0.004**	CURR*RACE (p=0.002) AGE (p<0.001) BFAT (p<0.001)
5	740	1.28 (1.10,1.49)**	0.002**	CURR*RACE (p=0.023) AGE (p<0.001) BFAT (p<0.001) RACE*FAMDIAB (p=0.032)
6[d]	739	1.23 (1.05,1.44)**	0.011**	CURR*RACE (p=0.025) AGE (p<0.001) BFAT (p<0.001) RACE*FAMDIAB (p=0.029)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interaction ($p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table N-2-15 for further analysis of this interaction.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

personality type, family history of diabetes, and the occupation-by-race interaction was retained in the adjusted analysis.

The association between initial dioxin and 2-hour postprandial glucose was not significant in the Model 2 unadjusted analysis (Table 18-31(c): p=0.390). In the adjusted analysis, there was a highly significant interaction between initial dioxin and race (Table 18-31(d): p=0.008). Results from stratified analysis on the interaction are found in Appendix Table N-2-15. When the initial dioxin-by-race interaction was removed from the final model, the association between initial dioxin and 2-hour postprandial glucose remained nonsignificant (p=0.112). Age, body fat, and personality type were significant covariates.

In the unadjusted Model 3 analysis of 2-hour postprandial glucose, significant differences were revealed between the high Ranch Hand category and the Comparison group and the low plus high Ranch Hand category and the Comparison group (Table 18-31(e): p=0.031, Est. RR=1.56 for high Ranch Hands vs. Comparisons and p=0.031, Est. RR=1.43 for low plus high Ranch Hands vs. Comparisons). For the Comparison category, 12.0 percent had an impaired 2-hour postprandial glucose level compared to 19.2 percent for high Ranch Hands and 17.5 percent for low plus high Ranch Hands. After adjusting for covariate information, significant differences between high and low plus high Ranch Hands and Comparisons remained (Table 18-31(f): p=0.023, Adj. RR=1.67 for high Ranch Hands vs. Comparisons and p=0.040, Adj. RR=1.44 for low plus high Ranch Hands vs. Comparisons). Age, personality type, body fat, and the race-by-family history of diabetes and occupation-by-race interactions were significant.

Highly significant positive associations between 2-hour postprandial glucose and current dioxin were revealed in each of the unadjusted Model 4 through 6 analyses (Table 18-31(g): p=0.001, Est. RR=1.27 for Model 4; p<0.001, Est. RR=1.28 for Model 5; and p=0.002, Est. RR=1.23 for Model 6). For the low, medium, and high categories of lipid-adjusted current dioxin, 10.2 percent, 13.2 percent, and 19.7 percent of the Ranch Hands had an impaired 2-hour postprandial glucose level. For whole-weight current dioxin, these percentages were 8.4, 14.5, and 20.6 for the low, medium, and high categories. For whole weight current dioxin adjusted for total lipids, the percentages were 8.5, 14.5, and 20.6 percent. The Model 4 adjusted analysis revealed a highly significant interaction between current dioxin and race (Table 18-31(h): p=0.002). Appendix Table N-2-15 presents results from further analysis of this interaction. Without the interaction in the final model, the association between current dioxin and 2-hour postprandial glucose remained significant (p=0.004, Adj. RR=1.27). Body fat and age also were retained. The interaction of current dioxin and race also was significant in the Model 5 and Model 6 adjusted analyses (p=0.023 and p=0.025 respectively). Analyses within the levels of race were performed for these interactions and results are shown in Appendix Table N-2-15. Deletion of the interaction from each of the final whole-weight current dioxin models showed a significant dioxin effect (p=0.002, Adj. RR=1.28 for Model 5 and p=0.011, Adj. RR=1.23 for Model 6). Covariates retained in the adjusted analyses included age, body fat, and the race-by-family history of diabetes interaction.

Fasting Urinary Glucose (All Participants)

Results from both the unadjusted and adjusted group analyses of fasting urinary glucose were nonsignificant (Table 18-32(a,b), p>0.39 for all contrasts). Covariates retained in the adjusted analysis included age, race, and the body fat-by-family history of diabetes interaction.

A significant association between fasting urinary glucose and initial dioxin was evident from the Model 2 unadjusted analyses (Table 18-32(c): p=0.023, Est. RR=1.39). Fasting urinary glucose was present in 2.3 percent, 3.5 percent, and 7.6 percent of the Ranch Hands for the low, medium, and high categories of initial dioxin respectively. After adjusting for race and the personality type-by-family history of diabetes and occupation-by-body fat interactions, the relationship between initial dioxin and fasting urinary glucose remained significant (Table 18-32(d): p=0.002, Adj. RR=1.97).

For Model 3, categorized dioxin was not significantly associated with fasting urinary glucose in the unadjusted analysis (Table 18-32(e): p>0.19 for all contrasts). The adjusted analysis revealed two significant categorized dioxin interactions, one with personality type and the other with body fat (Table 18-32(f): p=0.018 and p=0.011 respectively). Appendix Table N-2-16 presents the results from further analyses on these interactions. No significant differences between Comparisons and the four Ranch Hand categories were evident after the interactions were removed from the final model (p>0.14 for all contrasts). Additional covariates retained in the adjusted analysis included age and race.

Both the unadjusted and the adjusted analyses for Model 4 revealed a highly significant relationship between current dioxin and fasting urinary glucose (Table 18-32(g,h): p<0.001, Est. RR=1.58 for the unadjusted analysis and p<0.001, Adj. RR=1.70 for the adjusted analysis). For the low, medium, and high current dioxin categories, fasting urinary glucose was present in 1.0 percent, 3.4 percent, and 5.4 percent of the Ranch Hands. Age and the body fat-by-family history of diabetes interaction were significant covariates. Both the Model 5 and Model 6 unadjusted analyses of fasting urinary glucose found a highly significant association with current dioxin (Table 18-32: p<0.001, Est. RR=1.62 for Model 5 and p=0.001, Est. RR=1.48 for Model 6). For each analysis, the percentages of Ranch Hands with fasting urinary glucose present were 1.3, 2.0, and 6.4 for the low, medium, and high categories. In both adjusted analyses for Models 5 and 6, the interaction of current dioxin and personality type was significant (Table 18-32(h): p=0.044 for Model 5 and p=0.027 for Model 6). Analyses of these interactions are presented in Appendix Table N-2-16. In each case, the removal of the interaction from the final model revealed highly significant associations with current dioxin (p<0.001, Adj. RR=1.72 for Model 5 and p<0.001, Adj. RR=1.63 for Model 6). For Model 5, age and the body fat-by-family history of diabetes interaction were significant whereas, for Model 6, age and race were significant.

Fasting Urinary Glucose (Diabetics)

For diabetics, no significant differences between Ranch Hands and Comparisons were revealed in the Model 1 analyses of fasting urinary glucose in diabetics (Table 18-33(a,b): p>0.31 for both the unadjusted and the adjusted contrasts). Covariates retained in the adjusted analysis included diabetic severity and the body fat-by-family history of diabetes interaction.

Table 18-32.
Analysis of Fasting Urinary Glucose (All Participants)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Percent Present	Est. Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*948*	*3.1*	*1.00 (0.61,1.63)*	*0.999*
	Comparison	*1,276*	*3.1*		
Officer	Ranch Hand	365	2.5	0.88 (0.38,2.06)	0.938
	Comparison	502	2.8		
Enlisted Flyer	Ranch Hand	161	3.1	0.69 (0.23,2.09)	0.697
	Comparison	202	4.5		
Enlisted Groundcrew	Ranch Hand	422	3.6	1.28 (0.63,2.62)	0.621
	Comparison	572	2.8		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks[a]
All	*1.00 (0.61,1.66)*	*0.994*	AGE (p<0.001) RACE (p=0.049) BFAT*FAMDIAB (p<0.001)
Officer	0.83 (0.35,1.95)	0.664	
Enlisted Flyer	0.64 (0.19,2.20)	0.477	
Enlisted Groundcrew	1.37 (0.66,2.86)	0.397	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 18-32. (Continued)
Analysis of Fasting Urinary Glucose (All Participants)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Present	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	172	2.3	1.39 (1.05,1.85)	0.023
Medium	172	3.5		
High	172	7.6		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
503	1.97 (1.25,3.11)	0.002	RACE (p=0.044) OCC*BFAT (p=0.034) PERS*FAMDIAB (p=0.006)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 18-32. (Continued)
Analysis of Fasting Urinary Glucose (All Participants)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Percent Present	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,059	3.1		
Background RH	374	1.6	0.67 (0.27,1.62)	0.373
Low RH	257	3.1	0.84 (0.38,1.87)	0.673
High RH	259	5.8	1.53 (0.80,2.93)	0.195
Low plus High RH	516	4.5	1.19 (0.68,2.08)	0.542

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,058			DXCAT*PERS (p=0.018) DXCAT*BFAT (p=0.011) AGE (p=0.002) RACE (p=0.021)
Background RH	374	0.64 (0.26,1.56)**	0.327**	
Low RH	256	0.72 (0.32,1.64)**	0.431**	
High RH	259	1.66 (0.84,3.28)**	0.141**	
Low plus High RH	515	1.14 (0.64,2.02)**	0.661**	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Categorized dioxin-by-covariate interactions ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of these interactions; refer to Appendix Table N-2-16 for further analysis of these interactions.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 18-32. (Continued)
Analysis of Fasting Urinary Glucose (All Participants)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Present/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	1.0 (295)	3.4 (298)	5.4 (297)	1.58 (1.25,1.99)	<0.001
5	1.3 (300)	2.0 (295)	6.4 (295)	1.62 (1.30,2.01)	<0.001
6[c]	1.3 (299)	2.0 (295)	6.4 (295)	1.48 (1.17,1.87)	0.001

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	872	1.70 (1.30,2.23)	<0.001	AGE (p=0.004) BFAT*FAMDIAB (p=0.033)
5	871	1.72 (1.33,2.21)**	<0.001**	CURR*PERS (p=0.044) AGE (p=0.002) BFAT*FAMDIAB (p=0.035)
6[d]	888	1.63 (1.26,2.11)**	<0.001**	CURR*PERS (p=0.027) AGE (p=0.003) RACE (p=0.089)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table N-2-16 for further analysis of this interaction.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 18-33.
Analysis of Fasting Urinary Glucose (Diabetics)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Present**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	*Ranch Hand*	*142*	*20.4*	*0.95 (0.55,1.63)*	*0.949*
	Comparison	*178*	*21.3*		
Officer	Ranch Hand	55	16.4	0.61 (0.24,1.56)	0.428
	Comparison	58	24.1		
Enlisted Flyer	Ranch Hand	25	20.0	0.88 (0.25,3.07)	0.999
	Comparison	36	22.2		
Enlisted Groundcrew	Ranch Hand	62	24.2	1.36 (0.61,3.01)	0.585
	Comparison	84	19.0		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	*0.81 (0.44,1.48)*	*0.490*	DIABSEV (p<0.001) FAMDIAB*BFAT (p=0.008)
Officer	0.59 (0.21,1.66)	0.319	
Enlisted Flyer	0.60 (0.14,2.63)	0.501	
Enlisted Groundcrew	1.14 (0.48,2.74)	0.768	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 18-33. (Continued)
Analysis of Fasting Urinary Glucose (Diabetics)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Present	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	31	12.9	1.43 (1.03,2.00)	0.031
Medium	31	19.4		
High	34	38.2		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log$_2$ (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
96	2.13 (1.11,4.07)	0.009	RACE (p=0.050) DIABSEV (p=0.111) OCC*BFAT (p=0.002)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 18-33. (Continued)
Analysis of Fasting Urinary Glucose (Diabetics)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Present	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	147	21.8		
Background RH	42	14.3	0.71 (0.27,1.86)	0.483
Low RH	49	16.3	0.69 (0.29,1.62)	0.394
High RH	47	31.9	1.60 (0.77,3.35)	0.209
Low plus High RH	96	24.0	1.09 (0.59,2.02)	0.780

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	146			DXCAT*BFAT (p=0.001) AGE*OCC (p=0.016) AGE*BFAT (p=0.007) AGE*DIABSEV (p=0.028) RACE*OCC (p<0.001) RACE*BFAT (p=0.046) OCC*DIABSEV (p=0.007) FAMDIAB*BFAT (p=0.010)
Background RH	39	****	****	
Low RH	48	****	****	
High RH	46	****	****	
Low plus High RH	94	****	****	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

**** Categorized dioxin-by-covariate interaction ($p \leq 0.01$); adjusted relative risk, confidence interval, and p-value not presented; refer to Appendix Table N-2-17 for further analysis of this interaction.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 18-33. (Continued)
Analysis of Fasting Urinary Glucose (Diabetics)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Present/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	10.7 (28)	17.9 (56)	29.6 (54)	1.46 (1.11,1.92)	0.005
5	15.4 (26)	11.1 (54)	32.8 (58)	1.44 (1.13,1.84)	0.002
6[c]	15.4 (26)	11.1 (54)	32.8 (58)	1.37 (1.05,1.80)	0.018

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	138	1.49 (1.09,2.03)	0.010	DIABSEV (p<0.001)
5	138	1.44 (1.10,1.89)	0.005	DIABSEV (p<0.001)
6[d]	138	1.39 (1.03,1.88)	0.027	DIABSEV (p<0.001)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

A significant association between fasting urinary glucose and initial dioxin was seen in the unadjusted Model 2 analysis restricted to diabetics (Table 18-33(c): p=0.031, Est. RR=1.43). The association remained significant after adjusting for race, diabetic severity, and the occupation-by-body fat interaction (Table 18-33(d): p=0.009, Adj. RR=2.13). The percentage of diabetic Ranch Hands with fasting urinary glucose present were 12.9, 19.4, and 38.2 for the low, medium, and high initial dioxin categories.

For diabetics, no significant results were evident from the unadjusted Model 3 analysis of fasting urinary glucose (Table 18-33(e): p>0.20 for all contrasts). However, in the adjusted analysis, a highly significant interaction between categorized dioxin and body fat was disclosed (Table 18-33(f): p=0.001). Results of further analysis of this interaction are displayed in Appendix Table N-2-17. Significant in the adjusted analysis were age-by-occupation, age-by-body fat, age-by-diabetic severity, race-by-occupation, race-by-body fat, occupation-by-diabetic severity, and family history of diabetes-by-body fat interactions. After removing the interaction and body fat and occupation from the final model, no significant differences were found (Appendix Table N-3-20: p>0.46).

Each of the Model 4 through 6 unadjusted analyses restricted to diabetics showed highly significant associations between fasting urinary glucose and current dioxin (Table 18-33(g): p=0.005, Est. RR=1.46 for Model 4; p=0.002, Est. RR=1.44 for Model 5; and p=0.018, Est. RR=1.37 for Model 6). For Model 4, fasting urinary glucose was present in 10.7 percent of the diabetic Ranch Hands in the low category, 17.9 percent in the medium category, and 29.6 percent in the high category. In the low, medium, and high categories of current dioxin for both Models 5 and 6, 15.4 percent, 11.1 percent, and 32.8 percent of the diabetic Ranch Hands had fasting urinary glucose present. For each of the adjusted analyses, the association between fasting urinary glucose and current dioxin remained significant after adjusting for diabetic severity (Table 18-33(h): p=0.010, Adj. RR=1.49 for Model 4; p=0.005, Adj. RR=1.44 for Model 5; and p=0.027, Adj. RR=1.39 for Model 6).

Fasting Urinary Glucose (Nondiabetics)

Only one nondiabetic participant, a Comparison, had fasting urinary glucose present; therefore, for this variable, unadjusted and adjusted analyses restricted to nondiabetics were not performed for Models 1 through 6 in Table 18-34(a-h).

2-Hour Postprandial Urinary Glucose

The percentage of nondiabetic Ranch Hands with 2-hour postprandial urinary glucose present did not differ significantly from the percentage of nondiabetic Comparisons with 2-hour postprandial urinary glucose present in the unadjusted and adjusted Model 1 analyses (Table 18-35(a,b): p>0.57 for all contrasts). Significant covariates included age and occupation.

A marginally significant positive association between initial dioxin and 2-hour postprandial urinary glucose was evident in the Model 2 unadjusted analysis (Table 18-35(c): p=0.074, Est. RR=1.18). The tracheotomized levels of initial dioxin showed that for the low and medium dioxin categories, 19.1 percent and 15.6 percent of the nondiabetic Ranch Hands

Table 18-34.
Analysis of Fasting Urinary Glucose (Nondiabetics)

a) MODEL 1: RANCH HANDS vs. COMPARISONS

Occupational Category	Group	n	Percent Present
All	*Ranch Hand*	*806*	*0.0*
	Comparison	*1,098*	*0.1*
Officer	Ranch Hand	310	0.0
	Comparison	444	0.0
Enlisted Flyer	Ranch Hand	136	0.0
	Comparison	166	0.6
Enlisted Groundcrew	Ranch Hand	360	0.0
	Comparison	488	0.0

b) MODEL 2: RANCH HANDS — INITIAL DIOXIN

Initial Dioxin Category Summary Statistics		
Initial Dioxin	n	Percent Present
Low	141	0.0
Medium	141	0.0
High	138	0.0

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 18-34. (Continued)
Analysis of Fasting Urinary Glucose (Nondiabetics)

c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY		
Dioxin Category	n	Percent Present
Comparison	912	0.1
Background RH	332	0.0
Low RH	208	0.0
High RH	212	0.0
Low plus High RH	420	0.0

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

d) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN			
	Current Dioxin Category Percent Present/(n)		
Model[a]	Low	Medium	High
4	0.0 (267)	0.0 (242)	0.0 (243)
5	0.0 (274)	0.0 (241)	0.0 (237)
6	0.0 (273)	0.0 (241)	0.0 (237)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 18-35.
Analysis of 2-Hour Postprandial Urinary Glucose (Nondiabetics)

a) MODEL 1: RANCH HANDS vs. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Percent Present	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***806***	***18.6***	***1.02 (0.81,1.29)***	***0.895***
	Comparison	***1,095***	***18.3***		
Officer	Ranch Hand	308	14.9	1.10 (0.73,1.66)	0.731
	Comparison	443	13.8		
Enlisted Flyer	Ranch Hand	137	20.4	0.87 (0.50,1.50)	0.708
	Comparison	166	22.9		
Enlisted Groundcrew	Ranch Hand	361	21.1	1.02 (0.73,1.42)	0.992
	Comparison	486	20.8		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks[a]
All	***1.01 (0.80,1.28)***	***0.914***	AGE (p=0.002) OCC (p<0.001)
Officer	1.10 (0.72,1.66)	0.659	
Enlisted Flyer	0.85 (0.49,1.48)	0.578	
Enlisted Groundcrew	1.02 (0.73,1.43)	0.890	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 18-35. (Continued)
Analysis of 2-Hour Postprandial Urinary Glucose (Nondiabetics)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Present	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	141	19.1	1.18 (0.98,1.41)	0.074
Medium	141	15.6		
High	139	28.1		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[a]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
421	1.18 (0.98,1.41)	0.074	

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 18-35. (Continued)
Analysis of 2-Hour Postprandial Urinary Glucose (Nondiabetics)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Present	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	910	17.5		
Background RH	331	16.9	0.96 (0.69,1.35)	0.827
Low RH	208	18.8	1.11 (0.75,1.64)	0.604
High RH	213	23.0	1.39 (0.97,2.00)	0.076
Low plus High RH	421	20.9	1.25 (0.93,1.67)	0.137

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	910			AGE (p=0.005) OCC (p<0.001)
Background RH	331	1.09 (0.77,1.54)	0.620	
Low RH	208	1.08 (0.73,1.60)	0.699	
High RH	213	1.21 (0.83,1.77)	0.315	
Low plus High RH	421	1.15 (0.85,1.55)	0.366	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 18-35. (Continued)
Analysis of 2-Hour Postprandial Urinary Glucose (Nondiabetics)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[a]	Current Dioxin Category Percent Present/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) Est. Relative Risk (95% C.I.)[b]	p-Value
4	16.9 (267)	16.2 (241)	24.6 (244)	1.16 (1.03,1.32)	0.018
5	16.1 (273)	17.0 (241)	24.8 (238)	1.17 (1.05,1.31)	0.005
6[c]	16.2 (272)	17.0 (241)	24.8 (238)	1.11 (0.98,1.24)	0.095

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[a]	Analysis Results for Log_2 (Current Dioxin + 1) n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	752	1.13 (0.99,1.28)	0.075	BFAT (p=0.082)
5	752	1.17 (1.04,1.32)	0.011	AGE (p=0.096) BFAT (p=0.114)
6[d]	751	1.03 (0.90,1.19)**	0.636**	CURR*OCC (p=0.029) AGE (p=0.028) BFAT (p=0.051)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table N-2-18 for further analysis of this interaction.

Note: Model 4: Low = ≤8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤46 ppq; Medium = >46-128 ppq; High = >128 ppq.

had 2-hour postprandial urinary glucose present compared to 28.1 percent for the high dioxin category. The results of the Model 2 adjusted analysis were identical to those of the unadjusted analysis because no covariates were significant.

In the Model 3 unadjusted analysis, the difference in the percentages of nondiabetic participants with 2-hour postprandial urinary glucose present was marginally significant for high Ranch Hands versus Comparisons (Table 18-35(e): p=0.076, Est. RR=1.39, 23.0 vs. 17.5). After adjusting for age and occupation, the difference was no longer significant (Table 18-35(f): p=0.315). Likewise, the remaining three contrasts between Ranch Hands and Comparisons were nonsignificant (p>0.36). After removing occupation from the final model, however, high Ranch Hands were again found to differ significantly from Comparisons (Appendix Table N-3-21: p=0.048, Est. RR=1.45).

Significant positive associations between current dioxin and 2-hour postprandial urinary glucose were revealed in each of the Model 4 through 6 unadjusted analyses (Table 18-35(g): p=0.018, Est. RR=1.16 for Model 4; p=0.005, Est. RR=1.17 for Model 5; and p=0.095, Est. RR=1.11 for Model 6). For the low and medium categories of current dioxin for Model 4, 16.9 percent and 16.2 percent of nondiabetic Ranch Hands had 2-hour postprandial urinary glucose present compared to 24.6 percent for the high category. For the low dioxin categories of Models 5 and 6, 16.1 percent and 16.2 percent of nondiabetic Ranch Hands had 2-hojusted analysis, the interaction of current dioxin and occupation was significant (p=0.029). See Appendix Table N-2-18 for stratified results. After removing the interaction from the final model, no significant dioxin effect was evident (p=0.636). However, the removal of occupation and body fat from the final model caused the dioxin effect to once again become marginally significant (Appendix Table N-3-21: p=0.051, Adj. RR=1.13). Age and body fat were retained in the adjusted Model 6 analysis.

Serum Insulin (All Participants—Continuous)

In the unadjusted Model 1 analysis, overall mean serum insulin levels did not differ significantly between Ranch Hands and Comparisons (Table 18-36(a): p=0.581). However, when analyzed by occupation, there was a marginally significant difference between the two groups in the officer category (Diff. of Adj. Mean=4.03, p=0.096). Adjustment for covariate information disclosed significant group interactions with age and body fat (Table 18-36(b): p=0.029 and p=0.018 respectively). Appendix Table N-2-19 displays stratified results from analyses on each of these interactions. A significant difference in serum insulin means between Ranch Hands and Comparisons was found in obese participants (Appendix Table N-2-19: p=0.017, Diff. of Adj. Means=10.17), but not in lean or normal participants (p=0.380). Removal of the interactions from the final model did not reveal significant differences between Ranch Hands and Comparisons (Table 18-36(b): p>0.11 for all contrasts). Also significant in the adjusted analyses were fasting status and the age-by-body fat, race-by-occupation, personality type-by-family history of diabetes, and body fat-by-occupation interactions.

No significant association between initial dioxin and serum insulin was found in the unadjusted and adjusted Model 2 analyses (Table 18-36(c,d): p>0.11). Covariates retained in the adjusted analyses included fasting status and the age-by-body fat and body fat-by-

Table 18-36.
Analysis of Serum Insulin (mIU/ml) (All Participants) (Continuous)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Mean[ab]	Difference of Means (95% C.I.)[c]	p-Value[d]
All	*Ranch Hand*	*950*	*42.64*	*0.88 --*	*0.581*
	Comparison	*1,277*	*41.77*		
Officer	Ranch Hand	365	42.25	4.03 --	0.096
	Comparison	502	38.23		
Enlisted Flyer	Ranch Hand	162	42.65	-4.26 --	0.303
	Comparison	202	46.91		
Enlisted Groundcrew	Ranch Hand	423	42.68	-0.34 --	0.887
	Comparison	573	43.02		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Group	n	Adj. Mean[a]	Difference of Adj. Means (95% C.I.)[c]	p-Value[d]	Covariate Remarks[e]
All	*Ranch Hand*	*931*	*37.83***	*0.91 --***	0.472**	GROUP*AGE (p=0.029)
	Comparison	*1,258*	*36.92***			GROUP*BFAT (p=0.018)
Officer	Ranch Hand	359	44.11**	3.43 --**	0.134**	FAST (p<0.001)
	Comparison	499	40.68**			AGE*BFAT (p=0.010)
						RACE*OCC (p=0.005)
Enlisted Flyer	Ranch Hand	158	30.04**	-4.23 --**	0.114**	PERS*FAMDIAB (p=0.004)
	Comparison	197	34.27**			BFAT*OCC (p=0.039)
Enlisted Groundcrew	Ranch Hand	414	38.52**	1.22 --**	0.524**	
	Comparison	562	37.30**			

[a] Transformed from the natural logarithm scale.

[b] Adjusted for fasting status.

[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.

[d] P-values based on difference of means on natural logarithm scale.

[e] Covariates and associated p-values correspond to final model based on all participants with available data.

** Group-by-covariate interactions ($0.01 < p \leq 0.05$); adjusted mean, difference of adjusted means, and p-value derived from a model fitted after deletion of these interactions; refer to Appendix Table N-2-19 for further analysis of these interactions.

Table 18-36. (Continued)
Analysis of Serum Insulin (mIU/ml) (All Participants)
(Continuous)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[c]		
Initial Dioxin	n	Mean[ab]	Adj. Mean[ac]	R^2	Slope (Std. Error)[d]	p-Value
Low	173	42.29	41.17	0.218	0.0208 (0.0289)	0.472
Medium	172	46.09	44.25			
High	173	47.26	42.77			

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED						
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[d]			
Initial Dioxin	n	Adj. Mean[ae]	R^2	Adj. Slope (Std. Error)[d]	p-Value	Covariate Remarks
Low	173	37.92	0.347	0.0484 (0.0310)	0.119	FAST ($p<0.001$) AGE*BFAT ($p<0.001$) BFAT*OCC ($p=0.009$)
Medium	172	42.95				
High	173	44.45				

[a] Transformed from natural logarithm scale.

[b] Adjusted for fasting status.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and fasting status.

[d] Slope and standard error based on natural logarithm of serum insulin versus $\log_2$ (initial dioxin).

[e] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 18-36. (Continued)
Analysis of Serum Insulin (mIU/ml) (All Participants)
(Continuous)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED					
Dioxin Category	n	Mean[ab]	Adj. Mean[ac]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[d]	p-Value[e]
Comparison	1,060	43.17	39.93		
Background RH	374	37.95	38.39	-1.54 --	0.430
Low RH	258	46.65	42.23	2.30 --	0.327
High RH	260	49.93	42.91	2.99 --	0.208
Low plus High RH	518	48.27	42.57	2.64 --	0.148

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED					
Dioxin Category	n	Adj. Mean[af]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[d]	p-Value[e]	Covariate Remarks
Comparison	1,044	****			DXCAT*AGE (p=0.002) BFAT (p<0.001)
Background RH	368	****	****	****	FAST (p<0.001)
Low RH	251	****	****	****	RACE*OCC (p=0.002) OCC*PERS (p=0.024)
High RH	254	****	****	****	FAMDIAB*PERS (p=0.003)
Low plus High RH	505	****	****	****	

[a] Transformed from natural logarithm scale.

[b] Adjusting for fasting status.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and fasting status.

[d] Difference of adjusted means after transformation to original scale; confidence interval on difference of adjusted means not presented because analysis was performed on natural logarithm scale.

[e] P-value is based on difference of means on natural logarithm scale.

[f] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

**** Categorized dioxin-by-covariate interaction ($p \leq 0.01$); adjusted mean, difference of adjusted means, and p-value not presented; refer to Appendix Table N-2-19 for further analysis of this interaction.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 18-36. (Continued)
Analysis of Serum Insulin (mIU/ml) (All Participants)
(Continuous)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED						
	Current Dioxin Category Mean[ab]/(n)			Analysis Results for Log_2 (Current Dioxin + 1)		
Model[c]	Low	Medium	High	R^2	Slope (Std. Error)[d]	p-Value
4	34.64 (295)	43.68 (299)	48.92 (298)	0.113	0.0989 (0.0205)	<0.001
5	33.85 (300)	43.65 (296)	49.32 (296)	0.122	0.1008 (0.0175)	<0.001
6[e]	35.04 (299)	42.85 (296)	45.29 (296)	0.140	0.0726 (0.0186)	<0.001

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED							
	Current Dioxin Category Adjusted Mean[a]/(n)			Analysis Results for Log_2 (Current Dioxin + 1)			
Model[c]	Low	Medium	High	R^2	Adj. Slope (Std. Error)[d]	p-Value	Covariate Remarks
4	34.58 (290)	36.68 (294)	40.99 (290)	0.316	0.0374 (0.0220)	0.090	AGE (p<0.001) BFAT (p<0.001) FAST (p<0.001) OCC*FAMDIAB (p=0.013)
5	34.37 (296)	36.71 (290)	40.93 (288)	0.318	0.0455 (0.0186)	0.015	AGE (p<0.001) BFAT (p<0.001) FAST (p<0.001) OCC*FAMDIAB (p=0.015)
6[f]	35.92** (299)	36.75** (296)	38.57** (296)	0.328	0.0203 (0.0197)**	0.303**	CURR*BFAT (p=0.022) OCC (p=0.055) FAST (p<0.001) AGE*BFAT (p=0.034)

[a] Transformed from natural logarithm scale.

[b] Adjusted for fasting status.

[c] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[d] Slope and standard error based on natural logarithm of serum insulin versus log_2 (current dioxin + 1).

[e] Adjusted for log_2 total lipids and fasting status.

[f] Adjusted for log_2 total lipids and covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interaction ($0.01<p\leq0.05$); adjusted mean, adjusted slope, standard error, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table N-2-19 for further analysis of this interaction.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

occupation interactions. Once occupation and body fat were removed from the final model, the dioxin effect became significant (Appendix Table N-3-22: p=0.043, Slope=0.0607).

In the Model 3 unadjusted analysis, the difference in mean levels of serum insulin did not differ significantly between the four Ranch Hand categories and the Comparison group (Table 18-36(e): p>0.14 for all contrasts). The adjusted analysis revealed a highly significant interaction between categorized dioxin and age (Table 18-36(f): p=0.002). Stratified results for the interaction are presented in Appendix Table N-2-19. Because of the high significance level of the interaction, subsequent analysis removing it from the final model was not performed. Additional covariates retained in the adjusted analysis were body fat and fasting status and the race-by-occupation, occupation-by-personality type, and family history of diabetes-by-personality type interactions.

Each of the Model 4 through 6 unadjusted analyses revealed a highly significant association between serum insulin and current dioxin (Table 18-36(g): p<0.001 for each analysis). A similar trend in means was evident for each analysis, with mean serum insulin increasing with dioxin level. After adjusting for covariate information for Model 4, the association between current dioxin and serum insulin was marginally significant (Table 18-36(h): p=0.090, Slope=0.0374). Adjusted means for the low, medium, and high categories of current dioxin were 34.58 mIU/ml, 36.68 mIU/ml, 40.99 mIU/ml respectively. For the Model 5 adjusted analysis, there was again a significant association between serum insulin and current dioxin (p=0.015, Slope=0.0455). For this analysis, adjusted means were 34.37 mIU/ml, 36.71 mIU/ml, and 40.93 mIU/ml for the low, medium, and high dioxin categories. For both the Model 4 and 5 adjusted analyses, age, body fat, fasting status and the occupation-by-family history of diabetes interaction were significant. In the Model 6 adjusted analysis, the interaction of current dioxin and body fat was significant (p=0.022). Refer to Appendix Table N-2-19 for results from further analysis on this interaction. The association between serum insulin and current dioxin was nonsignificant after deletion of the interaction from the final model (p=0.303, Slope=0.0203). Occupation, fasting status, and the age-by-body fat interaction were retained in the adjusted analysis. For each of the Model 4 through 6 analyses, removal of body fat and occupation from the final model led to highly significant associations between serum insulin and current dioxin (Appendix Table N-3-22: p<0.001 for each analysis).

Serum Insulin (All Participants—Discrete)

In the Model 1 unadjusted analysis of serum insulin, no significant differences in the percentages of abnormalities between Ranch Hands and Comparisons were found (Table 18-37(a): p>0.20 for all analyses). In the adjusted analysis, two group interactions involving age and body fat were retained (Table 18-37(b): p=0.008 and p=0.020 respectively). Appendix Table N-2-20 presents the results from further analyses on these interactions. After removing the interactions from the final model, no significant group effect was disclosed (p>0.20 for all analyses). Other significant covariates included occupation and personality type.

Results from the unadjusted Model 2 analysis of serum insulin were nonsignificant (Table 18-37(c): p>0.24). Adjusting for age and body fat led to a marginally significant

Table 18-37.
Analysis of Serum Insulin (All Participants) (Discrete)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED									
			Percent			Low vs. Normal		High vs. Normal	
Occupational Category	Group	n	Abnormal Low	Normal	Abnormal High	Est. Relative Risk (95% C.I.)	p-Value	Est. Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*950*	*4.4*	*39.6*	*56.0*	*0.92 (0.61,1.40)*	*0.703*	*0.94 (0.79,1.12)*	*0.508*
	Comparison	*1,277*	*4.6*	*38.1*	*57.2*				
Officer	Ranch Hand	365	3.8	39.7	56.4	0.68 (0.35,1.34)	0.265	1.09 (0.82,1.44)	0.561
	Comparison	502	5.8	40.8	53.4				
Enlisted Flyer	Ranch Hand	162	4.3	37.7	58.0	1.05 (0.26,4.27)	0.947	0.75 (0.48,1.17)	0.206
	Comparison	202	3.5	31.7	64.9				
Enlisted Groundcrew	Ranch Hand	423	5.0	40.2	54.9	1.17 (0.40,3.40)	0.772	0.90 (0.69,1.16)	0.410
	Comparison	573	4.0	38.1	57.9				

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED					
	Low vs. Normal		High vs. Normal		
Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks[a]
All	0.92 (0.60,1.40)**	0.705**	0.96 (0.80,1.15)**	0.630**	GROUP*AGE (p=0.008) GROUP*BFAT (p=0.020) OCC (p=0.038) PERS (p=0.004)
Officer	0.73 (0.37,1.44)**	0.360**	1.08 (0.81,1.45)**	0.594**	
Enlisted Flyer	1.00 (0.33,3.03)**	0.995**	0.74 (0.47,1.18)**	0.207**	
Enlisted Groundcrew	1.11 (0.59,2.09)**	0.739**	0.94 (0.71,1.24)**	0.641**	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

** Group-by-covariate interactions ($p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of these interactions; refer to Appendix Table N-2-20 for further analysis of these interactions.

Table 18-37. (Continued)
Analysis of Serum Insulin (All Participants)
(Discrete)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED

Initial Dioxin Category	n	Abnormal Low (Percent)	Normal (Percent)	Abnormal High (Percent)	Low vs. Normal: Est. Relative Risk (95% C.I.)[b]	Low vs. Normal: p-Value	High vs. Normal: Est. Relative Risk (95% C.I.)[b]	High vs. Normal: p-Value
		Initial Dioxin Category Summary Statistics			*Analysis Results for Log_2 (Initial Dioxin)[a]*			
Low	173	3.5	38.7	57.8	0.80 (0.54,1.20)	0.242	0.96 (0.83,1.10)	0.571
Medium	172	5.8	29.7	64.5				
High	173	2.3	39.9	57.8				

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED

Analysis Results for Log_2 (Initial Dioxin)[c]

n	Low vs. Normal: Adj. Relative Risk (95% C.I.)[b]	Low vs. Normal: p-Value	High vs. Normal: Adj. Relative Risk (95% C.I.)[b]	High vs. Normal: p-Value	Covariate Remarks
518	0.67 (0.44,1.00)	0.064	1.10 (0.91,1.20)	0.406	AGE ($p<0.001$) BFAT ($p<0.001$)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 18-37. (Continued)
Analysis of Serum Insulin (All Participants)
(Discrete)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED								
		Percent			Low vs. Normal		High vs. Normal	
Dioxin Category	n	Abnormal Low	Normal	Abnormal High	Est. Relative Risk (95% C.I.)[ab]	p-Value	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,060	4.7	37.1	58.2				
Background RH	374	5.1	44.9	50.0	0.82 (0.47,1.44)	0.489	0.82 (0.64,1.05)	0.113
Low RH	258	4.3	36.8	58.9	0.92 (0.46,1.84)	0.804	0.99 (0.74,1.33)	0.944
High RH	260	3.5	35.4	61.2	0.82 (0.39,1.75)	0.611	0.97 (0.72,1.30)	0.835
Low plus High RH	518	3.9	36.1	60.0	0.87 (0.50,1.52)	0.626	0.98 (0.78,1.23)	0.858

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED						
		Low vs. Normal		High vs. Normal		
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,044					DXCAT*AGE (p=0.028) DXCAT*OCC (p=0.033) DXCAT*PERS (p=0.011) DXCAT*BFAT (p=0.006) FAMDIAB (p=0.122) RACE*PERS (p=0.039)
Background RH	368	0.72 (0.40,1.30)**	0.275**	0.81 (0.62,1.06)**	0.127**	
Low RH	251	0.82 (0.39,1.73)**	0.609**	0.95 (0.70,1.29)**	0.736**	
High RH	254	0.78 (0.35,1.74)**	0.540**	0.99 (0.72,1.37)**	0.972**	
Low plus High RH	505	0.80 (0.45,1.45)**	0.466**	0.97 (0.76,1.23)**	0.805**	

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of duty in SEA and change in body fat from the time of duty in SEA to the date of the blood draw for dioxin.
[c] Adjusted for percent body fat at the time of duty in SEA, change in body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Categorized dioxin-by-covariate interactions ($p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of these interactions; refer to Appendix Table N-2-20 for further analysis of these interactions.

Note: RH = Ranch Hand.
Comparison: Current Dioxin $\leq$ 10 ppt.
Background (Ranch Hand): Current Dioxin $\leq$ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin $\leq$ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 18-37. (Continued)
Analysis of Serum Insulin (All Participants)
(Discrete)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED									
	Current Dioxin Category Summary Statistics					Analysis Results for Log_2 (Current Dioxin + 1)			
			Percent			Low vs. Normal		High vs. Normal	
Model[a]	Current Dioxin Category	n	Abnormal Low	Normal	Abnormal High	Est. Relative Risk (95% C.I.)[b]	p-Value	Est. Relative Risk (95% C.I.)[b]	p-Value
4	Low	295	5.8	47.1	47.1	0.77 (0.60,0.99)	0.038	1.12 (1.02,1.24)	0.016
	Medium	299	4.0	37.5	58.5				
	High	298	3.4	34.9	61.7				
5	Low	300	6.0	46.7	47.3	0.80 (0.67,0.97)	0.021	1.14 (1.05,1.24)	0.002
	Medium	296	4.1	37.5	58.5				
	High	296	3.0	35.1	61.8				
6[c]	Low	299	6.0	46.5	47.5	0.79 (0.65,0.97)	0.021	1.12 (1.02,1.22)	0.013
	Medium	296	4.1	37.5	58.5				
	High	296	3.0	35.1	61.8				

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 18-37. (Continued)
Analysis of Serum Insulin (All Participants)
(Discrete)

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED						
	Analysis Results for Log_2 (Current Dioxin)					
		Low vs. Normal		High vs. Normal		
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	891	0.86 (0.68,1.10)**	0.223**	1.05 (0.94,1.17)**	0.407**	CURR*BFAT (p=0.039) AGE (p<0.001) BFAT*PERS (p=0.007)
5	891	0.88 (0.73,1.07)**	0.198**	1.07 (0.97,1.17)**	0.157**	CURR*BFAT (p=0.035) AGE (p<0.001) PERS*BFAT (p=0.007)
6[c]	890	0.86 (0.71,1.06)	0.156	1.04 (0.94,1.15)	0.451	PERS*BFAT (p=0.002) BFAT*AGE (p<0.001)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for $\log_2$ total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for $\log_2$ total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table N-2-20 for further analysis of this interaction.

negative association between initial dioxin and abnormally low serum insulin (Table 18-37(d): p=0.064, Adj. RR=0.67). After body fat was removed from the final model, the initial dioxin effect became nonsignificant (Table N-3-23: p=0.103).

The association between serum insulin and categorized dioxin was nonsignificant in the unadjusted Model 3 analysis (Table 18-37(e): p>0.11 for all analyses). The adjusted analysis revealed four significant categorized dioxin interactions involving age, occupation, personality type, and body fat (Table 18-37(f): p=0.028, p=0.033, p=0.011, and p=0.006 respectively). Results from further analyses on these interactions are found in Appendix Table N-2-20. Also significant in the adjusted analysis were family history of diabetes and the race-by-personality type interaction. The difference between Ranch Hands and Comparisons was nonsignificant after the interactions were deleted from the final model (Table 18-37(f): p>0.12 for all analyses). After removing body fat and occupation from the model, the relative risk of abnormally high serum insulin between background Ranch Hands and Comparisons became significant (Table N-3-23: p=0.040, Adj. RR=0.76).

In the unadjusted Model 4 analysis, a significant association between serum insulin and current dioxin was revealed for both the abnormally low and abnormally high categories of serum insulin (Table 18-37(g): p=0.038, Est. RR=0.77 for low vs. normal and p=0.016, Est. RR=1.12 for high vs. normal). In the adjusted analysis, a significant interaction between current dioxin and body fat was revealed (Table 18-37(h): p=0.039). Refer to Appendix Table N-2-20 for further analysis of this interaction. After removing the interaction from the final model, a significant dioxin effect was not seen (p>0.22 for both analyses). However, also removing body fat from the adjusted model caused the association with dioxin to become significant (Appendix Table N-3-23: p=0.016, Adj. RR=0.74 for low vs. normal and p=0.001, Adj. RR=1.19 for high vs. normal). Additional covariates significant in the adjusted analysis of Model 4 included age and the body fat-by-personality type interaction. The results of the Model 5 analyses of serum insulin closely parallel those of the Model 4 analyses. In the unadjusted analysis, a significant association between serum insulin and current dioxin was disclosed for both the abnormally low and abnormally high serum insulin categories (Table 18-37(g): p=0.021, Est. RR=0.80 for low vs. normal and p=0.002, Est. RR=1.14 for high vs. normal). The adjusted analysis revealed a significant interaction between current dioxin and body fat (Table 18-37(h): p=0.035). Appendix Table N-2-20 displays results from further analysis of this interaction. A significant association between serum insulin and current dioxin was not evident once the interaction was removed from the final model (p>0.15). However, removal of body fat caused the association between serum insulin and current dioxin to become significant (Appendix Table N-3-23: p=0.010, Adj. RR=0.79 for low vs. normal and p<0.001, Adj. RR=1.20 for high vs. normal). Age and the personality type-by-body fat interaction also were significant in the adjusted analysis of Model 5. The Model 6 unadjusted analysis of serum insulin revealed a significant association with current dioxin for both the abnormally low and abnormally high categories of serum insulin (Table 18-37(g): p=0.021, Est. RR=0.79 for low vs. normal and p=0.013, Est. RR=1.12 for high vs. normal). After adjusting for the body fat-by-age and personality type-by-body fat interactions, the association was nonsignificant (Table 18-37(h): p>0.15). However, removal of body fat from the final model caused the associations between serum insulin and current dioxin to become significant (Appendix Table N-3-23: p=0.008, Adj. RR=0.77 for low vs. normal and p=0.001, Adj. RR=1.17 for high vs. normal).

Serum Insulin (Diabetics—Continuous)

Neither the unadjusted nor the adjusted Model 1 analyses of serum insulin restricted to diabetics revealed a significant difference between Ranch Hands and Comparisons (Table 18-38(a,b): p>0.10 for all contrasts). Race, body fat, diabetic severity, fasting status, and the personality type-by-family history of diabetes interaction were significant in the adjusted analysis.

The Model 2 analyses of serum insulin in diabetics did not show a significant association between initial dioxin and serum insulin (Table 18-38(c,d): p>0.14 for both analyses). Race, body fat, diabetic severity, and fasting status were retained in the adjusted analysis.

In the Model 3 unadjusted analysis, the difference in mean serum insulin levels between diabetic Ranch Hands in the low category and diabetic Comparisons was marginally significant (Table 18-38(e): p=0.073, Diff. of Adj. Mean=15.93). For low Ranch Hands, mean serum insulin, adjusted for fasting status, was 68.73 mIU/ml compared to 52.80 mIU/ml for Comparisons. The remaining three contrasts were not significant (p>0.31). Likewise, in the adjusted analysis, mean serum insulin was significantly greater in low Ranch Hands (54.49 mIU/ml) than in Comparisons (40.11 mIU/ml) (Table 18-38(f): p=0.027, Diff. of Adj. Means=14.39). There were no significant differences between the other three Ranch Hand categories and the Comparison group (p>0.24). Significant covariates included race, body fat, diabetic severity, fasting status, and the personalty type-by-family history of diabetes interaction.

None of the Model 4, 5, and 6 unadjusted and adjusted analyses found a significant association between serum insulin in diabetics and current dioxin (Table 18-38(g,h): p>0.16 for all analyses). In each adjusted analysis, race, body fat, fasting status, and the personality type-by-family history of diabetes interaction were significant.

Serum Insulin (Diabetics—Discrete)

There were no diabetic Ranch Hands and only two diabetic Comparisons with abnormally low levels of serum insulin. Therefore, for diabetics, only differences between participants with abnormally high levels of serum insulin versus participants with normal levels of serum insulin were analyzed.

Neither the Model 1 unadjusted nor adjusted analyses of serum insulin revealed a significant difference between Ranch Hands and Comparisons (Table 18-39(a,b): p>0.14 for all analyses). Covariates retained in the adjusted analysis were occupation, diabetic severity, and personality type-by-family history of diabetes and body fat-by-family history of diabetes interactions.

In the Model 2 unadjusted analysis, a highly significant negative association between abnormally high serum insulin and initial dioxin was disclosed (Table 18-39(c): p=0.003, Est. RR=0.62). The percentage of diabetic participants with abnormally high levels of serum insulin was 61.3 percent and 77.4 percent for the low and medium dioxin categories versus 35.3 percent for the high category. Adjusting for covariate information led to significant

Table 18-38.
Analysis of Serum Insulin (mIU/ml) (Diabetics)
(Continuous)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	*Ranch Hand*	*142*	*59.78*	*9.08 --*	*0.102*
	Comparison	*179*	*50.70*		
Officer	Ranch Hand	55	70.41	14.74 --	0.163
	Comparison	58	55.68		
Enlisted Flyer	Ranch Hand	25	50.02	3.96 --	0.723
	Comparison	36	46.05		
Enlisted Groundcrew	Ranch Hand	62	55.56	5.98 --	0.445
	Comparison	85	49.58		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Group	n	Adj. Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]	Covariate Remarks[d]
All	*Ranch Hand*	*137*	*49.23*	*6.27 --*	0.149	RACE (p<0.001)
	Comparison	*177*	*42.96*			BFAT (p<0.001)
						DIABSEV (p<0.001)
Officer	Ranch Hand	53	53.16	9.72 --	0.206	FAST (p<0.001)
	Comparison	58	43.45			PERS*FAMDIAB
Enlisted Flyer	Ranch Hand	24	44.35	-2.05 --	0.838	(p=0.036)
	Comparison	34	46.39			
Enlisted Groundcrew	Ranch Hand	60	48.45	6.90 --	0.274	
	Comparison	85	41.54			

[a] Transformed from the natural logarithm scale.

[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.

[c] P-values based on difference of means on natural logarithm scale.

[d] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 18-38. (Continued)
Analysis of Serum Insulin (mIU/ml) (Diabetics) (Continuous)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[c]		
Initial Dioxin	n	Mean[ab]	Adj. Mean[ac]	R^2	Slope (Std. Error)[d]	p-Value
Low	31	67.73	60.55	0.537	-0.0911 (0.0619)	0.144
Medium	31	78.82	75.92			
High	34	34.17	47.25			

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED						
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[e]			
Initial Dioxin	n	Adj. Mean[ae]	R^2	Adj. Slope (Std. Error)[d]	p-Value	Covariate Remarks
Low	31	52.62	0.596	-0.0906 (0.0610)	0.142	RACE (p=0.047) BFAT (p=0.022) DIABSEV (p=0.626) FAST (p<0.001)
Medium	31	60.64				
High	34	42.27				

[a] Transformed from natural logarithm scale.

[b] Adjusted for fasting status.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and fasting status.

[d] Slope and standard error based on natural logarithm of serum insulin versus log_2 (initial dioxin).

[e] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 18-38. (Continued)
Analysis of Serum Insulin (mIU/ml) (Diabetics)
(Continuous)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Mean[ab]	Adj. Mean[ac]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[d]	p-Value[e]
Comparison	148	58.89	52.80		
Background RH	42	65.82	61.89	9.08 --	0.317
Low RH	49	73.35	68.73	15.93 --	0.073
High RH	47	41.99	50.42	-2.38 --	0.759
Low plus High RH	96	55.82	59.05	6.25 --	0.340

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Mean[af]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[d]	p-Value[e]	Covariate Remarks
Comparison	147	40.11			RACE (p<0.001) BFAT (p=0.007) DIABSEV (p=0.003) FAST (p<0.001) PERS*FAMDIAB (p=0.028)
Background RH	39	42.66	2.55 --	0.691	
Low RH	48	54.49	14.39 --	0.027	
High RH	46	38.42	-1.69 --	0.763	
Low plus High RH	94	45.60	5.49 --	0.245	

[a] Transformed from natural logarithm scale.

[b] Adjusted for fasting status.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and fasting status.

[d] Difference of adjusted means after transformation to original scale; confidence interval on difference of adjusted means not presented because analysis was performed on natural logarithm scale.

[e] P-value is based on difference of means on natural logarithm scale.

[f] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 18-38. (Continued)
Analysis of Serum Insulin (mIU/ml) (Diabetics)
(Continuous)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED						
	Current Dioxin Category Mean[ab]/(n)			Analysis Results for Log_2 (Current Dioxin + 1)		
Model[c]	Low	Medium	High	R^2	Slope (Std. Error)[d]	p-Value
4	50.04 (28)	54.73 (56)	47.03 (54)	0.478	-0.0442 (0.0501)	0.380
5	58.31 (26)	64.87 (54)	55.18 (58)	0.478	-0.0325 (0.0418)	0.438
6[e]	58.12 (26)	64.81 (54)	55.30 (58)	0.478	-0.0337 (0.0473)	0.477

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED							
	Current Dioxin Category Adjusted Mean[a]/(n)			Analysis Results for Log_2 (Current Dioxin + 1)			
Model[c]	Low	Medium	High	R^2	Adj. Slope (Std. Error)[d]	p-Value	Covariate Remarks
4	50.04 (26)	54.78 (55)	47.08 (52)	0.589	-0.0750 (0.0539)	0.166	RACE (p=0.039) BFAT (p<0.001) FAST (p<0.001) DIABSEV (p=0.155) PERS*FAMDIAB (p=0.029)
5	51.33 (24)	56.96 (53)	43.91 (56)	0.589	-0.0633 (0.0449)	0.161	RACE (p=0.038) BFAT (p<0.001) FAST (p<0.001) DIABSEV (p=0.149) PERS*FAMDIAB (p=0.038)
6[f]	48.29 (24)	55.77 (53)	45.61 (56)	0.591	-0.0449 (0.0507)	0.378	RACE (p=0.034) BFAT (p<0.001) FAST (p<0.001) DIABSEV (p=0.121) PERS*FAMDIAB (p=0.027)

[a] Transformed from natural logarithm scale.

[b] Adjusted for fasting status.

[c] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[d] Slope and standard error based on natural logarithm of serum insulin versus log_2 (current dioxin + 1).

[e] Adjusted for log_2 total lipids.

[f] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 18-39.
Analysis of Serum Insulin (Diabetics)
(Discrete)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Abnormal High**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	*Ranch Hand*	*142*	*60.6*	*1.21 (0.77,1.90)*	*0.472*
	Comparison	*177*	*55.9*		
Officer	Ranch Hand	55	74.5	1.79 (0.80,4.01)	0.222
	Comparison	58	62.1		
Enlisted Flyer	Ranch Hand	25	52.0	0.96 (0.34,2.71)	0.999
	Comparison	34	52.9		
Enlisted Groundcrew	Ranch Hand	62	51.6	0.95 (0.49,1.83)	0.999
	Comparison	85	52.9		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	*1.36 (0.79,2.33)*	*0.269*	OCC (p=0.011) DIABSEV (p<0.001) PERS*FAMDIAB (p=0.039) BFAT*FAMDIAB (p=0.032)
Officer	2.00 (0.78,5.15)	0.148	
Enlisted Flyer	0.77 (0.22,2.69)	0.686	
Enlisted Groundcrew	1.29 (0.59,2.82)	0.518	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 18-39. (Continued)
Analysis of Serum Insulin (Diabetics)
(Discrete)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log₂ (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Abnormal High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	31	61.3	0.62 (0.44,0.87)	0.003
Medium	31	77.4		
High	34	35.3		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
96	0.66 (0.43,1.03)**	0.057**	INIT*AGE (p=0.041) INIT*OCC (p=0.011) INIT*BFAT (p=0.015) RACE (p=0.130) DIABSEV (p=0.168)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Log_2 (initial dioxin)-by-covariate interactions ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of these interactions; refer to Appendix Table N-2-21 for further analysis of these interactions.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 18-39. (Continued)
Analysis of Serum Insulin (Diabetics)
(Discrete)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Percent Abnormal High	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	148	58.1		
Background RH	42	64.3	1.47 (0.70,3.08)	0.308
Low RH	49	67.3	1.62 (0.80,3.26)	0.177
High RH	47	46.8	0.61 (0.31,1.20)	0.150
Low plus High RH	96	57.3	0.99 (0.58,1.69)	0.968

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	148			DXCAT*AGE ($p=0.013$) RACE ($p=0.066$) PERS ($p=0.016$) BFAT ($p=0.001$) DIABSEV ($p<0.001$)
Background RH	42	1.16 (0.52,2.61)**	0.719**	
Low RH	49	1.96 (0.87,4.40)**	0.105**	
High RH	47	0.76 (0.35,1.66)**	0.491**	
Low plus High RH	96	1.21 (0.66,2.21)**	0.535**	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Categorized dioxin-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table N-2-21 for further analysis of this interaction.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤10 ppt.
Background (Ranch Hand): Current Dioxin ≤10 ppt.
Low (Ranch Hand): Current Dioxin >10 ppt, 10 ppt < Initial Dioxin ≤143 ppt.
High (Ranch Hand): Current Dioxin >10 ppt, Initial Dioxin >143 ppt.

Table 18-39. (Continued)
Analysis of Serum Insulin (Diabetics)
(Discrete)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Abnormal High/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	64.3 (28)	64.3 (56)	51.9 (54)	0.73 (0.58,0.93)	0.008
5	65.4 (26)	66.7 (54)	50.0 (58)	0.78 (0.63,0.95)	0.011
6[c]	65.4 (26)	66.7 (54)	50.0 (58)	0.78 (0.62,0.98)	0.029

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	138	****	****	CURR*BFAT (p=0.004) DIABSEV (p=0.154)
5	138	****	****	CURR*BFAT (p=0.003) DIABSEV (p=0.167)
6[d]	138	****	****	CURR*BFAT (p=0.003) DIABSEV (p=0.155)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

**** Log_2 (current dioxin + 1)-by-covariate interaction ($p \leq 0.01$); adjusted relative risk, confidence interval, and p-value not presented; refer to Appendix Table N-2-21 for further analysis of this interaction.

Note: Model 4: Low = ≤8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤46 ppq; Medium = >46-128 ppq; High = >128 ppq.

interactions between initial dioxin and age, occupation, and body fat (Table 18-39(d): p=0.041, 0.011, and 0.015). These interactions were further analyzed and subsequent results are shown in Appendix Table N-2-21. A marginally significant negative association remained after the interactions were removed from the final model (p=0.057, Adj. RR=0.66). Race and diabetic severity also were retained in the adjusted analysis.

No significant results were revealed in the unadjusted Model 3 analysis of serum insulin in diabetics (Table 18-39(e): p>0.15 for all contrasts). The interaction of categorized dioxin and age was significant in the adjusted analysis (Table 18-39(f): p=0.013). Supplemental analysis on the interaction was performed and findings are shown in Appendix Table N-2-21. Contrasts investigating differences between the four Ranch Hand categories and the Comparison group were nonsignificant after removing the interaction from the final model (p>0.10 for all analyses). Additional covariates significant in the adjusted analysis included race, personality type, body fat, and diabetic severity.

Each of the Model 4 through 6 unadjusted analyses of abnormally high serum insulin in diabetics revealed a significant negative association with current dioxin (Table 18-39(g): p=0.008, Est. RR=0.73 for Model 4; p=0.011, Est. RR=0.78 for Model 5; and p=0.029, Est. RR=0.78 for Model 6). The percentages of diabetics with abnormally high serum insulin levels in the low, medium, and high current dioxin categories were 64.3 percent, 64.3 percent, and 51.9 percent for Model 4. For Models 5 and 6, these percentages were 65.4 percent, 66.7 percent, and 50.0 percent respectively. In each of the adjusted Model 4, 5, and 6 analyses, a highly significant interaction between current dioxin and body fat was revealed (Table 18-39(h): p=0.004, p=0.003, p=0.003 respectively). In each model, a negative association was significant for obese diabetics and was nonsignificant for lean or normal diabetics. Refer to Appendix Table N-2-21 for further analyses of these interactions.

Serum Insulin (Nondiabetics—Continuous)

In the Model 1 unadjusted analysis of serum insulin in nondiabetics, no significant differences between Ranch Hands and Comparisons were revealed (Table 18-40(a): p>0.22 for all contrasts). In the adjusted analysis, the interaction of group and body fat was significant (Table 18-40(b): p=0.017). Stratified results from further investigation of this interaction are shown in Appendix Table N-2-22. After removing the interaction from the final model, overall and occupationally stratified differences between Ranch Hands and Comparisons were nonsignificant (p>0.11 for all contrasts). Age and the race-by-occupation, race-by-personality type, and personality type-by-family history of diabetes interactions were significant in the adjusted analysis.

The unadjusted Model 2 analysis detected a significant association between serum insulin in nondiabetics and initial dioxin (Table 18-40(c): p=0.048, Slope=0.0639). Serum insulin means, adjusted for percent body fat at time of duty in SEA and change in percent body fat from time of duty in SEA to date of the blood draw for dioxin, were 72.04 mIU/ml, 75.45 mIU/ml, and 82.16 mIU/ml for the low, medium, and high dioxin categories. The association remained significant after adjusting for interactions between age and body fat and between body fat and occupation (Table 18-40(d): p=0.035, Slope=0.0729). For the low, medium,

Table 18-40.
Analysis of Serum Insulin (mIU/ml) (Nondiabetics)
(Continuous)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Mean[ab]	Difference of Means (95% C.I.)[c]	p-Value[d]
All	*Ranch Hand*	*808*	*73.88*	*-0.29 --*	*0.923*
	Comparison	*1,098*	*74.17*		
Officer	Ranch Hand	310	69.90	3.83 --	0.374
	Comparison	444	66.07		
Enlisted Flyer	Ranch Hand	137	75.63	-9.64 --	0.225
	Comparison	166	85.27		
Enlisted Groundcrew	Ranch Hand	361	74.29	-1.70 --	0.703
	Comparison	488	75.99		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Group	n	Adj. Mean[ae]	Difference of Adj. Means (95% C.I.)[c]	p-Value[d]	Covariate Remarks[f]
All	*Ranch Hand*	*794*	*58.55***	*-0.08 -- ***	0.968**	GROUP*BFAT (p=0.017)
	Comparison	*1,081*	*58.64***			AGE (p<0.001)
						FAST (p=0.597)
Officer	Ranch Hand	306	64.42**	2.61 -- **	0.463**	RACE*OCC (p=0.024)
	Comparison	441	61.81**			RACE*PERS (p=0.029)
Enlisted Flyer	Ranch Hand	134	48.88**	-7.34 -- **	0.113**	PERS*FAMDIAB (p=0.037)
	Comparison	163	56.22**			
Enlisted Groundcrew	Ranch Hand	354	60.47**	0.65 -- **	0.839**	
	Comparison	477	59.82**			

[a] Transformed from the natural logarithm scale.

[b] Adjusted for fasting status.

[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.

[d] P-values based on difference of means on natural logarithm scale.

[e] Adjusted for fasting status and covariates specified under "Covariate Remarks" column.

[f] Covariates and associated p-values correspond to final model based on all participants with available data.

** Group-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted mean, difference of adjusted means, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table N-2-22 for further analysis of this interaction.

Table 18-40. (Continued)
Analysis of Serum Insulin (mIU/ml) (Nondiabetics)
(Continuous)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	142	69.93	72.04	0.121	0.0639 (0.0321)	0.048
Medium	141	73.83	75.45			
High	139	86.58	82.16			

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED						
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[d]			
Initial Dioxin	n	Adj. Mean[ad]	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
Low	142	66.29	0.272	0.0729 (0.0344)	0.035	AGE*BFAT (p=0.007) BFAT*OCC (p=0.036)
Medium	141	72.67				
High	139	81.29				

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Slope and standard error based on natural logarithm of serum insulin versus log_2 (initial dioxin).

[d] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 18-40. (Continued)
Analysis of Serum Insulin (mIU/ml) (Nondiabetics)
(Continuous)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Mean[ab]	Adj. Mean[ac]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[d]	p-Value[e]
Comparison	912	77.13	67.20		
Background RH	332	66.22	62.62	-4.58 --	0.170
Low RH	209	79.03	67.08	-0.12 --	0.977
High RH	213	93.63	74.68	7.48 --	0.083
Low plus High RH	422	86.09	70.81	3.61 --	0.266

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Mean[af]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[d]	p-Value[e]	Covariate Remarks
Comparison	897	58.41**			DXCAT*AGE (p=0.040) BFAT (p<0.001) FAST (p=0.417) RACE*OCC (p=0.012) OCC*PERS (p=0.011) FAMDIAB*PERS (p=0.045)
Background RH	329	55.85**	-2.56 -- **	0.365**	
Low RH	203	56.80**	-1.61 -- **	0.631**	
High RH	208	64.38**	5.97 -- **	0.104**	
Low plus High RH	411	60.51**	2.10 -- **	0.437**	

[a] Transformed from natural logarithm scale.

[b] Adjusted for fasting status.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and fasting status.

[d] Difference of adjusted means after transformation to original scale; confidence interval on difference of adjusted means not presented because analysis was performed on natural logarithm scale.

[e] P-value is based on difference of means on natural logarithm scale.

[f] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Categorized dioxin-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted mean, difference of adjusted means, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table N-2-22 for further analysis of this interaction.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤10 ppt.
Background (Ranch Hand): Current Dioxin ≤10 ppt.
Low (Ranch Hand): Current Dioxin >10 ppt, 10 ppt < Initial Dioxin ≤143 ppt.
High (Ranch Hand): Current Dioxin >10 ppt, Initial Dioxin >143 ppt.

Table 18-40. (Continued)
Analysis of Serum Insulin (mIU/ml) (Nondiabetics)
(Continuous)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED						
	Current Dioxin Category Mean[ab]/(n)			Analysis Results for Log_2 (Current Dioxin + 1)		
Model[c]	Low	Medium	High	R^2	Slope (Std. Error)[d]	p-Value
4	36.01 (267)	44.15 (243)	52.82 (244)	0.044	0.1259 (0.0218)	<0.001
5	35.80 (274)	44.22 (242)	54.68 (238)	0.059	0.1263 (0.0187)	<0.001
6[e]	38.12 (273)	44.23 (242)	51.13 (238)	0.089	0.0960 (0.0196)	<0.001

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED							
	Current Dioxin Category Adjusted Mean[a]/(n)			Analysis Results for Log_2 (Current Dioxin + 1)			
Model[c]	Low	Medium	High	R^2	Adj. Slope (Std. Error)[d]	p-Value	Covariate Remarks
4	34.54 (267)	34.47 (242)	41.15 (244)	0.273	0.0529 (0.0235)	0.025	AGE (p<0.001) BFAT (p<0.001) FAST (p=0.127) OCC*PERS (p=0.025)
5	34.41 (274)	35.24 (241)	42.33 (238)	0.278	0.0646 (0.0200)	0.001	AGE (p<0.001) BFAT (p<0.001) FAST (p=0.141) OCC*PERS (p=0.030)
6[f]	36.51 (273)	35.47 (241)	39.63 (238)	0.303	0.0351 (0.0208)	0.092	AGE (p<0.001) BFAT (p<0.001) FAST (p=0.138) OCC*PERS (p=0.036)

[a] Transformed from natural logarithm scale.

[b] Adjusted for fasting status.

[c] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[d] Slope and standard error based on natural logarithm of serum insulin versus log_2 (current dioxin + 1).

[e] Adjusted for log_2 total lipids.

[f] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤46 ppq; Medium = >46-128 ppq; High = >128 ppq.

and high dioxin categories, respective adjusted means were 66.29 mIU/ml, 72.67 mIU/ml, and 81.29 mIU/ml.

A marginally significant difference between high Ranch Hands and Comparisons was evident from the Model 3 unadjusted analysis of serum insulin in nondiabetics (Table 18-40(e): p=0.083, Diff. of Adj. Means=7.48). For high Ranch Hands, mean serum insulin was 74.68 mIU/ml compared to 67.20 mIU/ml for Comparisons. A significant interaction between categorized dioxin and age was revealed in the adjusted Model 3 analysis (Table 18-40(f): p=0.040). Appendix Table N-2-22 displays results from further analysis of the interaction. After removing the interaction from the final model, no significant differences between Ranch Hands and Comparisons were seen (Table 18-40(f): p>0.10 for all contrasts). Removal of occupation and body fat from the final model led to a significant difference between older high Ranch Hands and older Comparisons (Appendix Table N-4-8: p=0.048, Diff. of Adj. Means=15.07) that was not significant with occupation and body fat in the final model. The race-by-occupation, occupation-by-personality type, and family history of diabetes-by-personality type interactions were significant in the adjusted analysis.

Highly significant associations between serum insulin and current dioxin were seen in each of the Model 4 through 6 unadjusted analyses (Table 18-40(g): p<0.001, Slope=0.1259 for Model 4; p<0.001, Slope=0.1263 for Model 5; and p<0.001, Slope=0.0960 for Model 6). Mean serum insulin levels increased with current dioxin in each analysis. After adjusting for age, body fat, fasting status, and the occupation-by-personality type interaction, significant dioxin effects remained for Models 4 and 5 and a marginally significant dioxin effect remained for Model 6 (Table 18-40(h): p=0.025, Slope=0.0529 for Model 4; p=0.001, Slope=0.0646 for Model 5; and p=0.092, Slope=0.0351 for Model 6). For Model 4, adjusted means were 34.54 mIU/ml, 34.47 mIU/ml, 41.15 mIU/ml for the low, medium, and high dioxin categories. For Model 5, the adjusted means were 34.41 mIU/ml, 35.24 mIU/ml, and 42.33 mIU/ml, and for Model 6, the adjusted means were 36.51 mIU/ml, 35.47 mIU/ml, and 39.63 mIU/ml.

Serum Insulin (Nondiabetics—Discrete)

The percentages of nondiabetic Ranch Hands with either abnormally high or abnormally low levels of serum insulin did not differ significantly from the corresponding percentage of nondiabetic Comparisons in the Model 1 unadjusted analysis (Table 18-41(a): p>0.15 for all contrasts). In the adjusted analyses, significant interactions between group and age and between group and body fat were disclosed (Table 18-41(b): p=0.007 and p=0.044 respectively). See Appendix Table N-2-23 for additional information on these interactions. Ranch Hands and Comparisons did not differ significantly after the interactions were removed from the final model (p>0.11 for all contrasts). Occupation, family history of diabetes, and the race-by-personality type and body fat-by-personality type interactions also were significant in the adjusted analysis.

In the Model 2 unadjusted analysis of serum insulin restricted to nondiabetics, no significant association with initial dioxin was revealed (Table 18-41(c): p>0.21). The interaction of initial dioxin and occupation was significant in the adjusted analysis (Table 18-41(d): p=0.028). After this interaction was deleted from the final model, a

Table 18-41.
Analysis of Serum Insulin (Nondiabetics)
(Discrete)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED									
			Percent			Low vs. Normal		High vs. Normal	
Occupational Category	Group	n	Abnormal Low	Normal	Abnormal High	Est. Relative Risk (95% C.I.)	p-Value	Est. Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*808*	*5.2*	*39.6*	*55.2*	*0.94 (0.62,1.44)*	*0.782*	*0.90 (0.75,1.09)*	*0.287*
	Comparison	*1,098*	*5.2*	*37.3*	*57.6*				
Officer	Ranch Hand	310	4.5	42.3	53.2	0.67 (0.34,1.33)	0.254	0.99 (0.74,1.34)	0.966
	Comparison	444	6.5	41.2	52.3				
Enlisted Flyer	Ranch Hand	137	5.1	35.8	59.1	1.37 (0.31,6.06)	0.677	0.70 (0.43,1.15)	0.157
	Comparison	166	3.0	28.9	68.1				
Enlisted Groundcrew	Ranch Hand	361	5.8	38.8	55.4	1.16 (0.40,3.37)	0.784	0.89 (0.67,1.18)	0.404
	Comparison	488	4.7	36.5	58.8				

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED					
	Low vs. Normal		High vs. Normal		
Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks[a]
All	*0.87 (0.56,1.34)***	*0.529***	*0.88 (0.72,1.08)***	*0.217***	GROUP*AGE (p=0.007) GROUP*BFAT (p=0.044) OCC (p=0.001) FAMDIAB (p=0.065) RACE*PERS (p=0.034) PERS*BFAT (p=0.031)
Officer	0.64 (0.32,1.28)**	0.203**	0.95 (0.69,1.30)**	0.731**	
Enlisted Flyer	1.08 (0.31,3.81)**	0.903**	0.66 (0.39,1.11)**	0.116**	
Enlisted Groundcrew	1.09 (0.57,2.06)**	0.795**	0.91 (0.67,1.25)**	0.569**	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

** Group-by-covariate interaction ($p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table N-2-23 for further analysis of this interaction.

Table 18-41. (Continued)
Analysis of Serum Insulin (Nondiabetics)
(Discrete)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED								
Initial Dioxin Category Summary Statistics					Analysis Results for Log_2 (Initial Dioxin)[a]			
		Percent			Low vs. Normal		High vs. Normal	
Initial Dioxin Category	n	Abnormal Low	Normal	Abnormal High	Est. Relative Risk (95% C.I.)[b]	p-Value	Est. Relative Risk (95% C.I.)[b]	p-Value
Low	142	4.2	38.7	57.0	0.88 (0.59,1.30)	0.550	1.10 (0.94,1.30)	0.215
Medium	141	7.1	31.2	61.7				
High	139	2.9	33.8	63.3				

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED					
Analysis Results for Log_2 (Initial Dioxin)[c]					
	Low vs. Normal		High vs. Normal		
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
422	0.90 (0.55,1.50)**	0.685**	1.20 (1.00,1.50)**	0.047**	INIT*OCC (p=0.028) AGE (p<0.001) BFAT (p<0.001)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

** Log_2 (initial dioxin)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted risk, confidence interval, and p-value derived from a model fitted after deletion of these interactions; refer to Appendix Table N-2-23 for further analysis of this interaction.

Table 18-41. (Continued)
Analysis of Serum Insulin (Nondiabetics)
(Discrete)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED								
		Percent			Low vs. Normal		High vs. Normal	
Dioxin Category	n	Abnormal Low	Normal	Abnormal High	Est. Relative Risk (95% C.I.)[ab]	p-Value	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	912	5.3	36.5	58.2				
Background RH	332	5.7	46.1	48.2	0.84 (0.48,1.49)	0.560	0.75 (0.57,0.99)	0.040
Low RH	209	5.3	37.8	56.9	0.95 (0.47,1.93)	0.893	0.89 (0.64,1.24)	0.490
High RH	213	4.2	31.5	64.3	0.98 (0.46,2.11)	0.960	1.10 (0.79,1.54)	0.571
Low plus High RH	422	4.7	34.6	60.7	0.97 (0.55,1.70)	0.907	0.99 (0.77,1.28)	0.934

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED						
		Low vs. Normal		High vs. Normal		
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	897					DXCAT*OCC (p=0.003) AGE (p<0.001) PERS (p=0.019) BFAT (p<0.001) FAMDIAB (p=0.026)
Background RH	329	****	****	****	****	
Low RH	203	****	****	****	****	
High RH	208	****	****	****	****	
Low plus High RH	411	****	****	****	****	

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of duty in SEA and change in body fat from the time of duty in SEA to the date of the blood draw for dioxin.
[c] Adjusted for percent body fat at the time of duty in SEA, change in body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

**** Categorized dioxin-by-covariate interaction ($p \leq 0.01$); adjusted relative risk, confidence interval, and p-value not presented; refer to Appendix Table N-2-23 for further analysis of this interaction.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 18-41. (Continued)
Analysis of Serum Insulin (Nondiabetics)
(Discrete)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED									
	Current Dioxin Category Summary Statistics					Analysis Results for Log_2 (Current Dioxin + 1)			
			Percent			Low vs. Normal		High vs. Normal	
Model[a]	Current Dioxin Category	n	Abnormal Low	Normal	Abnormal High	Est. Relative Risk (95% C.I.)[b]	p-Value	Est. Relative Risk (95% C.I.)[b]	p-Value
4	Low	267	6.4	48.3	45.3	0.83 (0.64,1.07)	0.148	1.24 (1.11,1.38)	<0.001
	Medium	243	4.9	37.9	57.2				
	High	244	4.1	32.0	63.9				
5	Low	274	6.6	47.8	45.6	0.85 (0.70,1.03)	0.105	1.26 (1.14,1.38)	<0.001
	Medium	242	5.0	38.4	56.6				
	High	238	3.8	31.5	64.7				
6[c]	Low	273	6.6	47.6	45.8	0.83 (0.68,1.03)	0.089	1.22 (1.10,1.34)	<0.001
	Medium	242	5.0	38.4	56.6				
	High	238	3.8	31.5	64.7				

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

Note: Model 4: Low = $\leq$ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = $\leq$ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 18-41. (Continued)
Analysis of Serum Insulin (Nondiabetics)
(Discrete)

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED						
	Analysis Results for Log_2 (Current Dioxin)					
		Low vs. Normal		High vs. Normal		
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	753	0.93 (0.72,1.20)	0.581	1.19 (1.06,1.35)	0.005	PERS*BFAT (p=0.008) AGE (p<0.001)
5	753	0.93 (0.76,1.15)	0.520	1.22 (1.09,1.36)	<0.001	PERS*BFAT (p=0.008) AGE (p<0.001)
6[c]	752	****	****	****	****	CURR*AGE (p<0.001) PERS*BFAT (p=0.011)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

**** Log_2 (current dioxin + 1)-by-covariate interaction ($p \leq 0.01$); adjusted relative risk, confidence interval, and p-value not presented; refer to Appendix Table N-2-23 for further analysis of this interaction.

significant positive relationship between abnormally high serum insulin and initial dioxin was revealed (p=0.047, Adj. RR=1.20). The stratified results from analysis on the initial dioxin-by-occupation interaction are shown in Appendix Table N-2-23. The covariates age and body fat also were significant.

The Model 3 unadjusted analysis restricted to nondiabetics revealed a significant negative difference between background Ranch Hands and Comparisons with abnormally high levels of serum insulin (Table 18-41(e): p=0.040, Est. RR=0.75). Of the background Ranch Hands, 48.2 percent had abnormally high serum insulin levels compared to 58.2 percent for Comparisons. The adjusted analysis revealed a highly significant interaction between categorized dioxin and occupation (Table 18-41(f): p=0.003). Stratified results of this interaction are found in Appendix Table N-2-23. Significant differences between background, low, and high Ranch Hands and Comparisons were found for enlisted flyers but not for officers and enlisted groundcrew. Age, personality type, body fat, and family history of diabetes also were retained in the adjusted analysis.

In each of the Model 4 through 6 analyses, a highly significant positive association between current dioxin and serum insulin was revealed for nondiabetics with abnormally high serum insulin levels (Table 18-41(g): p<0.001, Est. RR=1.24 for Model 4; p<0.001, Est. RR=1.26 for Model 5; and p<0.001, Est. RR=1.22 for Model 6). In addition, in Model 6, a marginally significant negative association with current dioxin was found for nondiabetic participants with abnormally low serum insulin levels (p=0.089, Est. RR=0.83). The adjusted analysis for Model 4 revealed a significant dioxin effect for participants with abnormally high levels of serum insulin (Table 18-41(h): p=0.005, Adj. RR=1.19). This result also was seen in the Model 5 adjusted analysis (p<0.001, Adj. RR=1.22). Age and the personality type-by-body fat interaction were retained in Models 4 and 5. After removing body fat from each of the final models, marginally significant negative associations between current dioxin and serum insulin were seen for nondiabetics with abnormally low serum insulin levels (Appendix Table N-3-27: p=0.093, Adj. RR=0.80 for Model 4 and p=0.069, Adj. RR=0.83 for Model 5). In the Model 6 adjusted analysis, the interaction of current dioxin and age was highly significant (p<0.001). Results from additional analyses on the interaction term are shown in Appendix Table N-2-23. Also retained in the adjusted analysis was the personality type-by-body fat interaction. Without body fat and the current dioxin-by-age interaction in Model 6, the association between serum insulin and current dioxin was significantly negative for abnormally low serum insulin (Appendix Table N-3-27: p=0.047, Adj. RR=0.81) and was significantly positive for abnormally high serum insulin (p<0.001, Adj. RR=1.30).

Serum Glucagon (All Participants—Continuous)

In the Model 1 unadjusted analysis, no significant overall difference in mean serum glucagon levels was evident for Ranch Hands versus Comparisons (Table 18-42(a): p=0.316). However, stratified analyses by occupation revealed a significant negative difference between Ranch Hands and Comparisons in the enlisted flyer category (p=0.031, Diff. of Adj. Means= -3.71). After adjusting for age, race, occupation, body fat, and fasting status, similar results were revealed. Significant differences between Ranch Hands and Comparisons were evident only when examined within the enlisted flyer category (Table 18-42(b): p=0.028, Diff. of

Table 18-42.
Analysis of Serum Glucagon (pg/ml) (All Participants)
(Continuous)

a) MODEL 1: RANCH HANDS vs. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Mean[ab]	Difference of Means (95% C.I.)[c]	p-Value[d]
All	*Ranch Hand*	*827*	*61.81*	*-0.73 --*	*0.316*
	Comparison	*1,104*	*62.54*		
Officer	Ranch Hand	315	61.60	-0.51 --	0.660
	Comparison	430	62.11		
Enlisted Flyer	Ranch Hand	145	59.33	-3.71 --	0.031
	Comparison	186	63.03		
Enlisted Groundcrew	Ranch Hand	367	62.95	0.28 --	0.802
	Comparison	488	62.68		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Group	n	Adj. Mean[a]	Difference of Adj. Means (95% C.I.)[c]	p-Value[d]	Covariate Remarks[e]
All	*Ranch Hand*	*827*	*59.82*	*-0.69 --*	0.326	AGE (p<0.001)
	Comparison	*1,104*	*60.50*			RACE (p=0.086)
Officer	Ranch Hand	315	59.08	-0.53 --	0.632	OCC (p=0.007)
	Comparison	430	59.61			BFAT (p=0.002)
Enlisted Flyer	Ranch Hand	145	57.37	-3.62 --	0.028	FAST (p<0.001)
	Comparison	186	60.99			
Enlisted Groundcrew	Ranch Hand	367	62.02	0.36 --	0.735	
	Comparison	488	61.66			

[a] Transformed from the natural logarithmic scale.

[b] Adjusted for fasting status.

[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithmic scale.

[d] P-values based on difference of means on natural logarithmic scale.

[e] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 18-42. (Continued)
Analysis of Serum Glucagon (pg/ml) (All Participants)
(Continuous)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[c]		
Initial Dioxin	n	Mean[ab]	Adj. Mean[ac]	R^2	Slope (Std. Error)[d]	p-Value
Low	150	59.30	59.10	0.047	0.0079 (0.0092)	0.392
Medium	149	62.87	62.72			
High	153	61.82	61.62			

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED						
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[d]			
Initial Dioxin	n	Adj. Mean[ae]	R^2	Adj. Slope (Std. Error)[d]	p-Value	Covariate Remarks
Low	150	58.21**	0.084**	0.0003 (0.0105)**	0.974**	INIT*OCC (p=0.020) FAST (p<0.001) BFAT*RACE (p=0.029)
Medium	149	61.11**				
High	153	59.42**				

[a] Transformed from natural logarithm scale.

[b] Adjusted for fasting status.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and fasting status.

[d] Slope and standard error based on natural logarithm of serum glucagon versus $\log_2$ (initial dioxin).

[e] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Log_2 (initial dioxin)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted mean, adjusted slope, standard error, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table N-2-24 for further analysis of this interaction.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 18-42. (Continued)
Analysis of Serum Glucagon (pg/ml) (All Participants)
(Continuous)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED					
Dioxin Category	n	Mean[ab]	Adj. Mean[ac]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[d]	p-Value[e]
Comparison	957	63.07	62.70		
Background RH	336	61.37	61.40	-1.30 --	0.197
Low RH	228	61.99	61.47	-1.24 --	0.289
High RH	224	63.24	62.60	-0.10 --	0.931
Low plus High RH	452	62.61	62.03	-0.67 --	0.457

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED					
Dioxin Category	n	Adj. Mean[af]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[d]	p-Value[e]	Covariate Remarks
Comparison	944	60.81**			DXCAT*FAMDIAB (p=0.009) AGE (p<0.001) RACE (p=0.124) OCC (p=0.067) FAST (p<0.001)
Background RH	330	59.66**	-1.16 -- **	0.251**	
Low RH	223	59.72**	-1.10 -- **	0.337**	
High RH	218	61.03**	0.21 -- **	0.858**	
Low plus High RH	441	60.36**	-0.45 -- **	0.616**	

[a] Transformed from natural logarithm scale.

[b] Adjusted for fasting status.

[c] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[d] Difference of adjusted means after transformation to original scale; confidence interval on difference of adjusted means not presented because analysis was performed on natural logarithm scale.

[e] P-value is based on difference of means on natural logarithm scale.

[f] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Categorized dioxin-by-covariate interaction ($p \leq 0.05$); adjusted mean, difference of adjusted means, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table N-2-24 for further analysis of this interaction.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤10 ppt.
Background (Ranch Hand): Current Dioxin ≤10 ppt.
Low (Ranch Hand): Current Dioxin >10 ppt, 10 ppt < Initial Dioxin ≤143 ppt.
High (Ranch Hand): Current Dioxin >10 ppt, Initial Dioxin >143 ppt.

Table 18-42. (Continued)
Analysis of Serum Glucagon (pg/ml) (All Participants)
(Continuous)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED						
	Current Dioxin Category Mean[ab]/(n)			Analysis Results for Log_2 (Current Dioxin + 1)		
Model[c]	Low	Medium	High	R^2	Slope (Std. Error)[d]	p-Value
4	60.04 (263)	60.54 (266)	63.00 (259)	0.051	0.0111 (0.0062)	0.073
5	59.81 (267)	61.09 (263)	62.58 (258)	0.054	0.0120 (0.0053)	0.023
6[e]	60.13 (266)	60.99 (263)	62.00 (258)	0.057	0.0084 (0.0057)	0.140

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED							
	Current Dioxin Category Adjusted Mean[a]/(n)			Analysis Results for Log_2 (Current Dioxin + 1)			
Model[c]	Low	Medium	High	R^2	Adj. Slope (Std. Error)[d]	p-Value	Covariate Remarks
4	**** (258)	**** (262)	**** (251)	0.085	****	****	CURR*FAMDIAB (p=0.005) AGE (p=0.001) RACE (p=0.051) OCC (p=0.018) FAST (p<0.001)
5	56.69 (267)	57.86 (263)	59.36 (258)	0.078	0.0019 (0.0059)	0.044	AGE (p<0.001) RACE (p=0.053) OCC (p=0.012) FAST (p<0.001)
6[f]	57.14 (266)	57.94 (263)	58.98 (258)	0.080	0.0084 (0.0064)	0.187	AGE (p=0.001) RACE (p=0.069) OCC (p=0.011) FAST (p<0.001)

[a] Transformed from natural logarithm scale.

[b] Adjusted for fasting status.

[c] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[d] Slope and standard error based on natural logarithm of serum glucagon versus log_2 (current dioxin + 1).

[e] Adjusted for log_2 total lipids.

[f] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

**** Log_2 (current dioxin + 1)-by-covariate interaction ($p \leq 0.01$); adjusted mean, adjusted slope, standard error and p-value not presented; refer to Appendix Table N-2-24 for further analysis of this interaction.

Note: Model 4: Low = ≤8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Adj. Means=-3.62), where adjusted mean serum glucagon levels were again higher for Comparisons (60.99 pg/ml) than for Ranch Hands (57.37 pg/ml).

Neither the Model 2 nor Model 3 unadjusted analysis of serum glucagon disclosed any significant results (Table 18-42(c,e): p>0.19 for all analyses). The Model 2 adjusted analysis revealed a significant interaction between initial dioxin and occupation (Table 18-42(d): p=0.020). Appendix Table N-2-24 displays results from further analysis on this interaction. The association between serum glucagon and initial dioxin was nonsignificant after the interaction was removed from the final model (p=0.974). Fasting status and the body fat-by-race interaction also were significant in the adjusted analysis. In the Model 3 adjusted analysis, a significant interaction between categorized dioxin and family history of diabetes was revealed (Table 18-42(f): p=0.009). Refer to Appendix Table N-2-24 for further analysis of this interaction. Subsequent analysis with the interaction removed revealed nonsignificant differences between the four Ranch Hand categories and Comparisons. Additional covariates retained in the Model 3 adjusted analysis included age, race, occupation, and fasting status.

Marginally significant and significant positive associations between current dioxin and serum glucagon were evident from the Model 4 and Model 5 unadjusted analyses (Table 18-42(g): p=0.073, Slope=0.0111 for Model 4 and p=0.023, Slope=0.0120 for Model 5). In each analysis, mean serum glucagon levels increased with increasing dioxin levels. The Model 6 unadjusted analysis had nonsignificant results (p=0.140). A highly significant interaction between current dioxin and family history of diabetes was disclosed in the Model 4 adjusted analysis (Table 18-42(h): p=0.005). Results from further analysis of this interaction are presented in Appendix Table N-2-24. Because of its high significance level (p<0.01), analysis with the interaction deleted from the final model was not performed. In the Model 5 adjusted analysis, current dioxin was significantly associated with serum glucagon (p=0.044, Slope=0.0019) with adjusted means again increasing with the low, medium, and high levels of current dioxin. Further adjustment for total lipids in the Model 6 adjusted analysis revealed nonsignificant results (p=0.187). However, removal of occupation from the final model led to a significant dioxin effect (Appendix Table N-3-28: p=0.040, Slope=0.0119). In each of the Model 4 through 6 adjusted analyses, age, race, and occupation were significant covariates.

Serum Glucagon (All Participants—Discrete)

Results from both the Model 1 unadjusted and adjusted analyses of serum glucagon were nonsignificant (Table 18-43(a,b): p>0.16 for all contrasts). The adjusted analysis retained age, occupation, and body fat.

The association between dioxin and serum glucagon was not significant in the Model 2 and Model 3 unadjusted analyses (Table 18-43(c,e): p>0.16). Adjusting for age and race did not lead to significant results in the Model 2 adjusted analysis (Table 18-43(d): p=0.930). Adjusted analyses of Model 3 were precluded by the sparse number of participants with abnormally high serum glucagon levels.

Table 18-43.
Analysis of Serum Glucagon (All Participants)
(Discrete)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Abnormal High**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***827***	***0.4***	***4.02 (0.42,38.68)***	***0.426***
	Comparison	***1,104***	***0.1***		
Officer	Ranch Hand	315	0.0	--	--
	Comparison	430	0.0		
Enlisted Flyer	Ranch Hand	145	0.0	--	--
	Comparison	186	0.0		
Enlisted Groundcrew	Ranch Hand	367	0.8	4.01 (0.42,38.75)	0.428
	Comparison	488	0.2		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***4.63 (0.45,47.67)***	***0.161***	AGE (p=0.003) OCC (p=0.007) BFAT (p=0.006)
Officer	--	--	
Enlisted Flyer	--	--	
Enlisted Groundcrew	4.63 (0.45,47.50)	0.161	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

--: Adjusted relative risk, confidence interval, and p-value not presented due to the sparse number of abnormalities.

Table 18-43. (Continued)
Analysis of Serum Glucagon (All Participants)
(Discrete)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Abnormal High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	150	0.0	0.71 (0.22,2.32)	0.546
Medium	149	1.3		
High	153	0.0		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
452	0.93 (0.16,5.22)	0.930	AGE (p=0.019) RACE (p=0.040)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 18-43. (Continued)
Analysis of Serum Glucagon (All Participants)
(Discrete)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Abnormal High	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	957	0.1		
Background RH	336	0.3	4.64 (0.28,77.40)	0.287
Low RH	228	0.9	5.67 (0.49,65.60)	0.165
High RH	224	0.0	--	--
Low plus High RH	452	0.4	2.64 (0.23,30.57)	0.439

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ab]	p-Value	Covariate Remarks
Comparison	957			
Background RH	336	--	--	
Low RH	228	--	--	
High RH	224	--	--	
Low plus High RH	452	--	--	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

--: Adjusted relative risk, confidence interval, and p-value not presented due to the sparse number of abnormalities.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 18-43. (Continued)
Analysis of Serum Glucagon (All Participants)
(Discrete)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Abnormal High/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	0.4 (263)	0.0 (266)	0.8 (259)	0.98 (0.45,2.14)	0.964
5	0.4 (267)	0.4 (263)	0.4 (258)	0.96 (0.49,1.86)	0.900
6[c]	0.4 (266)	0.4 (263)	0.4 (258)	1.05 (0.51,2.16)	0.894

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	788	0.95 (0.36,2.54)	0.920	AGE (p=0.033) BFAT (p=0.069)
5	788	0.90 (0.37,2.20)	0.821	AGE (p=0.035) BFAT (p=0.065)
6[d]	787	1.00 (0.38,2.64)	0.998	AGE (p=0.037) BFAT (p=0.078)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

No significant associations between current dioxin and serum glucagon were revealed from the unadjusted and adjusted analyses for Models 4, 5, and 6 (Table 18-43(g,h): p>0.82 for all analyses). Age and body fat were significant in each of the three adjusted analyses.

Serum Glucagon (Diabetics—Continuous)

Differences between diabetic Ranch Hands and Comparisons were not significant in the Model 1 unadjusted analysis of serum glucagon (Table 18-44(a): p≥0.31 for all contrasts). However, adjusting for covariate information led to two significant group interactions: group-by-body fat and group-by-diabetic severity (Table 18-44(b): p=0.031 and p<0.001 respectively). These interactions were further analyzed and subsequent results are presented in Appendix Table N-2-25. Significant group differences were not evident from analyses with the interactions removed from the final model (Table 18-44(b): p>0.15 for all contrasts). The adjusted analysis also retained interactions between age and occupation and between body fat and occupation.

Both the Model 2 and Model 3 unadjusted analyses restricted to diabetics led to nonsignificant associations between serum glucagon and dioxin (Table 18-44(c,e): p≥0.44). For Model 2, adjustment for occupation, body fat, and diabetic severity did not lead to a significant dioxin effect (Table 18-44(d): p=0.237). Two significant dioxin interactions involving body fat and diabetic severity were found in the Model 3 adjusted analysis of serum glucagon (Table 18-44(f): p=0.026 and p<0.001 respectively). Appendix Table N-2-25 shows results from additional analyses on these interactions. Removal of the interactions from the final model did not reveal significant differences between Ranch Hands and Comparisons (Table 18-44(f): p>0.23 for all contrasts). Age and the body fat-by-occupation interaction were retained in the Model 3 adjusted analysis.

None of the Model 4 through 6 analyses of serum glucagon restricted to diabetics disclosed any significant results (Table 18-44(g,h): p>0.58 for all analyses). Occupation and diabetic severity were significant in each of the three adjusted analyses.

Serum Glucagon (Diabetics—Discrete)

Restricted to diabetics, the results of the Model 1 unadjusted analysis of serum glucagon were not significant (Table 18-45(a): p>0.40). An adjusted analysis was not performed due to the sparse number of abnormalities (three Ranch Hands and one Comparison).

The Model 2 unadjusted and adjusted analyses of serum glucagon did not reveal a significant association with initial dioxin for diabetic participants (Table 18-45(c,d): p>0.56). Likewise, the Model 3 unadjusted analysis did not show any significant differences between Ranch Hands and Comparisons (Table 18-45(e): p>0.14). Because of the sparse number of abnormalities (one Comparison, one background Ranch Hand, and two low Ranch Hands) an adjusted Model 3 analysis was not conducted.

The results of the Model 4 through 6 analyses of serum glucagon restricted to diabetics were not significant (Table 18-45(g,h): p>0.12 for all analyses). In the Model 4 adjusted analysis, occupation was significant while age, race, occupation, body fat and family history

Table 18-44.
Analysis of Serum Glucagon (pg/ml) (Diabetics)
(Continuous)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Mean[ab]	Difference of Means (95% C.I.)[c]	p-Value[d]
All	*Ranch Hand*	*125*	*66.62*	*1.33 --*	*0.599*
	Comparison	*160*	*65.30*		
Officer	Ranch Hand	50	66.11	1.92 --	0.640
	Comparison	54	64.19		
Enlisted Flyer	Ranch Hand	21	60.11	-5.72 --	0.313
	Comparison	32	65.83		
Enlisted Groundcrew	Ranch Hand	54	69.84	3.96 --	0.310
	Comparison	74	65.88		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Group	n	Adj. Mean[a]	Difference of Adj. Means (95% C.I.)[c]	p-Value[d]	Covariate Remarks[e]
All	*Ranch Hand*	*125*	*70.27***	*0.58 -- ***	0.824**	GROUP*BFAT (p=0.031) GROUP*DIABSEV (p<0.001) AGE*OCC (p=0.040) BFAT*OCC (p=0.032) FAST (p=0.637)
	Comparison	*160*	*69.68***			
Officer	Ranch Hand	50	70.22**	1.61 -- **	0.709**	
	Comparison	54	68.62**			
Enlisted Flyer	Ranch Hand	21	62.58**	-8.31 -- **	0.158**	
	Comparison	32	70.89**			
Enlisted Groundcrew	Ranch Hand	54	75.61**	3.67 -- **	0.372**	
	Comparison	74	71.94**			

[a] Transformed from the natural logarithm scale.

[b] Adjusted for fasting status.

[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.

[d] P-values based on difference of means on natural logarithm scale.

[e] Covariates and associated p-values correspond to final model based on all participants with available data.

** Group-by-covariate interaction (p≤0.05); adjusted mean, difference of adjusted means, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table N-2-25 for further analysis of this interaction.

Table 18-44. (Continued)
Analysis of Serum Glucagon (pg/ml) (Diabetics)
(Continuous)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[c]		
Initial Dioxin	n	Mean[ab]	Adj. Mean[ac]	R^2	Slope (Std. Error)[d]	p-Value
Low	28	61.71	61.52	0.022	-0.0169 (0.0259)	0.515
Medium	27	71.76	71.65			
High	28	63.33	63.62			

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED						
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[e]			
Initial Dioxin	n	Adj. Mean[ae]	R^2	Adj. Slope (Std. Error)[d]	p-Value	Covariate Remarks
Low	28	62.79	0.153	-0.0338 (0.0283)	0.237	OCC (p=0.030) BFAT (p=0.139) DIABSEV (p=0.353) FAST (p=0.473)
Medium	27	71.46				
High	28	59.87				

[a] Transformed from natural logarithm scale.

[b] Adjusted for fasting status.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin and fasting status.

[d] Slope and standard error based on natural logarithm of serum glucagon versus log_2 (initial dioxin).

[e] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 18-44. (Continued)
Analysis of Serum Glucagon (pg/ml) (Diabetics)
(Continuous)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED					
Dioxin Category	n	Mean[ab]	Adj. Mean[ac]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[d]	p-Value[e]
Comparison	132	66.31	66.15		
Background RH	38	67.16	68.71	2.56 --	0.534
Low RH	45	66.58	66.28	0.13 --	0.972
High RH	38	63.82	63.14	-3.02 --	0.440
Low plus High RH	83	65.30	64.82	-1.33 --	0.657

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED					
Dioxin Category	n	Adj. Mean[af]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[d]	p-Value[e]	Covariate Remarks
Comparison	132	68.44**			DXCAT*BFAT (p=0.026) DXCAT*DIABSEV (p<0.001) AGE (p=0.039) FAST (p=0.461) BFAT*OCC (p=0.025)
Background RH	38	72.37**	3.93 -- **	0.363**	
Low RH	45	68.82**	0.38 -- **	0.920**	
High RH	38	63.62**	-4.82 -- **	0.233**	
Low plus High RH	83	66.39**	-2.05 -- **	0.497**	

[a] Transformed from natural logarithm scale.

[b] Adjusted for fasting status.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin and fasting status.

[d] Difference of adjusted means after transformation to original scale; confidence interval on difference of adjusted means not presented because analysis was performed on natural logarithm scale.

[e] P-value is based on difference of means on natural logarithm scale.

[f] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Categorized dioxin-by-covariate interaction ($p \leq 0.05$); adjusted mean, difference of adjusted means, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table N-2-25 for further analysis of this interaction.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 18-44. (Continued)
Analysis of Serum Glucagon (pg/ml) (Diabetics)
(Continuous)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED						
	Current Dioxin Category Mean[ab]/(n)			Analysis Results for Log_2 (Current Dioxin + 1)		
Model[c]	Low	Medium	High	R^2	Slope (Std. Error)[d]	p-Value
4	66.39 (27)	63.96 (49)	67.66 (45)	0.015	-0.0070 (0.0184)	0.705
5	65.94 (25)	65.56 (47)	66.11 (49)	0.014	0.0009 (0.0153)	0.952
6[e]	68.10 (25)	66.19 (47)	64.43 (49)	0.029	-0.0093 (0.0171)	0.587

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED							
	Current Dioxin Category Adjusted Mean[a]/(n)			Analysis Results for Log_2 (Current Dioxin + 1)			
Model[c]	Low	Medium	High	R^2	Adj. Slope (Std. Error)[d]	p-Value	Covariate Remarks
4	64.68 (27)	64.59 (49)	68.26 (45)	0.096	0.0008 (0.0215)	0.970	OCC (p=0.113) DIABSEV (p=0.111) FAST (p=0.693)
5	64.23 (25)	66.37 (47)	66.63 (49)	0.099	0.0095 (0.0173)	0.585	OCC (p=0.121) DIABSEV (p=0.084) FAST (p=0.703)
6[f]	66.17 (25)	67.01 (47)	64.92 (49)	0.106	-0.0005 (0.0201)	0.978	OCC (p=0.104) DIABSEV (p=0.142) FAST (p=0.688)

[a] Transformed from natural logarithm scale.

[b] Adjusted for fasting status.

[c] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[d] Slope and standard error based on natural logarithm of serum glucagon versus log_2 (current dioxin + 1).

[e] Adjusted for log_2 total lipids.

[f] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 18-45.
Analysis of Serum Glucagon (Diabetics)
(Discrete)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Percent Abnormal High	Est. Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*125*	*2.4*	*3.91 (0.40,38.05)*	*0.449*
	Comparison	*160*	*0.6*		
Officer	Ranch Hand	50	0.0	--	--
	Comparison	54	0.0		
Enlisted Flyer	Ranch Hand	21	0.0	--	--
	Comparison	32	0.0		
Enlisted Groundcrew	Ranch Hand	54	5.6	4.29 (0.43,42.46)	0.403
	Comparison	74	1.4		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks[a]
All	--	--	
Officer	--	--	
Enlisted Flyer	--	--	
Enlisted Groundcrew	--	--	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

--: Adjusted relative risk, confidence interval, and p-value not presented due to the sparse number of abnormalities.

Table 18-45. (Continued)
Analysis of Serum Glucagon (Diabetics)
(Discrete)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Abnormal High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	28	0.0	0.72 (0.22,2.37)	0.566
Medium	27	7.4		
High	28	0.0		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
83	1.26 (0.21,7.72)	0.808	AGE (p=0.072) RACE (p=0.064) DIABSEV (p=0.024)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 18-45. (Continued)
Analysis of Serum Glucagon (Diabetics)
(Discrete)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Abnormal High	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	132	0.8		
Background RH	38	2.6	8.33 (0.42,167.13)	0.166
Low RH	45	4.4	6.44 (0.51,80.67)	0.149
High RH	38	0.0	--	--
Low plus High RH	83	2.4	2.57 (0.22,30.32)	0.453

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ab]	p-Value	Covariate Remarks
Comparison	132			
Background RH	38	--	--	
Low RH	45	--	--	
High RH	38	--	--	
Low plus High RH	83	--	--	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

--: Adjusted relative risk, confidence interval, and p-value not presented due to the sparse number of abnormalities.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤10 ppt.
Background (Ranch Hand): Current Dioxin ≤10 ppt.
Low (Ranch Hand): Current Dioxin >10 ppt, 10 ppt < Initial Dioxin ≤143 ppt.
High (Ranch Hand): Current Dioxin >10 ppt, Initial Dioxin >143 ppt.

Table 18-45. (Continued)
Analysis of Serum Glucagon (Diabetics)
(Discrete)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[a]	Current Dioxin Category Percent Abnormal High/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) Est. Relative Risk (95% C.I.)[b]	p-Value
4	3.7 (27)	0.0 (49)	4.4 (45)	0.87 (0.40,1.89)	0.722
5	4.0 (25)	2.1 (47)	2.0 (49)	0.87 (0.48,1.56)	0.643
6[c]	4.0 (25)	2.1 (47)	2.0 (49)	1.03 (0.51,2.06)	0.938

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[a]	n	Analysis Results for Log_2 (Current Dioxin + 1) Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	121	0.78 (0.41,1.48)	0.433	OCC (p=0.056) DIABSEV (p=0.665)
5	116	0.39 (0.07,2.19)	0.128	AGE (p=0.024) RACE (p=0.141) OCC (p=0.020) BFAT (p=0.100) FAMDIAB (p=0.131) DIABSEV (p=0.936)
6[d]	121	1.03 (0.53,1.99)	0.927	DIABSEV (p=0.772)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤46 ppq; Medium = >46-128 ppq; High = >128 ppq.

of diabetes were significant in the Model 5 adjusted analysis. No covariates were significant in Model 6.

Serum Glucagon (Nondiabetics—Continuous)

In the Model 1 unadjusted analysis of serum glucagon restricted to nondiabetics, no significant overall difference in mean serum glucagon levels between Ranch Hands and Comparisons was revealed (Table 18-46(a): p=0.146). However, analyses within the levels of occupation revealed a marginally significant negative difference between the two groups in the enlisted flyer category (p=0.067, Diff. of Means=-2.98). This result remained marginally significant after adjusting for age, race, and occupation (Table 18-46(b): p=0.059, Diff. of Adj. Means=-2.93). The remaining contrasts between Ranch Hands and Comparisons in Model 1 were not significant.

A marginally significant positive association between serum glucagon and initial dioxin was disclosed in the unadjusted analysis for Model 2 (Table 18-46(c): p=0.060, Slope=0.0180). After an adjustment was made for family history of diabetes, the association remained significant (Table 18-46(d): p=0.041, Slope=0.0199). Adjusted means were 52.25 pg/ml, 54.47 pg/ml, and 55.28 pg/ml for the low, medium, and high dioxin categories respectively.

In the Model 3 unadjusted analysis, the mean serum glucagon level for nondiabetic background Ranch Hands was marginally lower than that of nondiabetic Comparisons (Table 18-46(e): p=0.087, Diff. of Adj. Means=-1.60). This result remained after adjustment for age and race (Table 18-46(f): p=0.051, Diff. of Adj. Means=-1.76). The serum glucagon adjusted mean for background Ranch Hands was 54.48 pg/ml compared to 56.24 pg/ml for Comparisons.

Each of the Model 4 through 6 unadjusted analyses of serum glucagon restricted to nondiabetics revealed a significant association with current dioxin (Table 18-46(g): p=0.025, Slope=0.0143 for Model 4; p=0.013, Slope=0.0136 for Model 5; and p=0.047, Slope=0.0117 for Model 6). In each analysis, serum glucagon levels increased with dioxin. Likewise, in each of the adjusted Model 4 through 6 analyses, the association between serum glucagon and current dioxin was significant (Table 18-46(h): p=0.044, Slope=0.0147, for Model 4; p=0.027, Slope=0.0138 for Model 5; and p=0.065, Slope=0.0123 for Model 6). Age, race, and occupation were retained in each analysis.

Serum Glucagon (Nondiabetics—Discrete)

There were no nondiabetic participants with abnormally high serum glucagon levels; therefore, the Model 1 through Model 6 analyses for this variable were not performed (Table 18-47(a-h).

α-1-C Hemoglobin (All Participants—Continuous)

The unadjusted and adjusted analyses of α-1-C hemoglobin did not reveal a significant group effect (Table 18-48(a,b): p>0.34). Covariates retained in the adjusted analysis include

Table 18-46.
Analysis of Serum Glucagon (pg/ml) (Nondiabetics)
(Continuous)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Mean[ab]**	**Difference of Means (95% C.I.)[c]**	**p-Value[d]**
All	*Ranch Hand*	*702*	*57.09*	*-0.99 --*	*0.146*
	Comparison	*944*	*58.09*		
Officer	Ranch Hand	265	56.61	-1.01 --	0.355
	Comparison	376	57.62		
Enlisted Flyer	Ranch Hand	124	55.24	-2.98 --	0.067
	Comparison	154	58.23		
Enlisted Groundcrew	Ranch Hand	313	57.73	-0.19 --	0.851
	Comparison	414	57.92		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED						
Occupational Category	**Group**	**n**	**Adj. Mean[a]**	**Difference of Adj. Means (95% C.I.)[c]**	**p-Value[d]**	**Covariate Remarks[e]**
All	*Ranch Hand*	*702*	*54.55*	*-0.96 --*	0.139	AGE (p<0.001)
	Comparison	*944*	*55.51*			RACE (p=0.021)
Officer	Ranch Hand	265	53.83	-0.97 --	0.346	OCC (p=0.025)
	Comparison	376	54.80			FAST (p=0.687)
Enlisted Flyer	Ranch Hand	124	52.82	-2.93 --	0.059	
	Comparison	154	55.76			
Enlisted Groundcrew	Ranch Hand	313	56.28	-0.17 --	0.865	
	Comparison	414	56.45			

[a] Transformed from the natural logarithm scale.

[b] Adjusted for fasting status.

[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.

[d] P-values based on difference of means on natural logarithm scale.

[e] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 18-46. (Continued)
Analysis of Serum Glucagon (pg/ml) (Nondiabetics)
(Continuous)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	122	53.36	53.34	0.011	0.0180 (0.0095)	0.060
Medium	122	55.53	55.55			
High	125	56.31	56.30			

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED						
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[d]			
Initial Dioxin	n	Adj. Mean[ad]	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
Low	120	52.25	0.026	0.0199 (0.0097)	0.041	FAMDIAB (p=0.022)
Medium	119	54.47				
High	121	55.28				

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Slope and standard error based on natural logarithm of serum glucagon versus $\log_2$ (initial dioxin).

[d] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 18-46. (Continued)
Analysis of Serum Glucagon (pg/ml) (Nondiabetics)
(Continuous)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED					
Dioxin Category	**n**	**Mean[ab]**	**Adj. Mean[ac]**	**Difference of Adj. Mean vs. Comparisons (95% C.I.)[d]**	**p-Value[e]**
Comparison	825	58.37	58.17		
Background RH	298	56.64	56.57	-1.60 --	0.087
Low RH	183	56.77	56.54	-1.63 --	0.146
High RH	186	59.10	58.79	0.62 --	0.585
Low plus High RH	369	57.93	57.66	-0.51 --	0.560

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED					
Dioxin Category	**n**	**Adj. Mean[af]**	**Difference of Adj. Mean vs. Comparisons (95% C.I.)[d]**	**p-Value[e]**	**Covariate Remarks**
Comparison	825	56.24			AGE (p=0.005) RACE (p=0.024) FAST (p=0.616)
Background RH	298	54.48	-1.76 --	0.051	
Low RH	183	54.75	-1.49 --	0.171	
High RH	186	57.23	0.99 --	0.371	
Low plus High RH	369	55.98	-0.25 --	0.767	

[a] Transformed from natural logarithm scale.

[b] Adjusted for fasting status.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and fasting status.

[d] Difference of adjusted means after transformation to original scale; confidence interval on difference of adjusted means not presented because analysis was performed on natural logarithm scale.

[e] P-value is based on difference of means on natural logarithm scale.

[f] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 18-46. (Continued)
Analysis of Serum Glucagon (pg/ml) (Nondiabetics)
(Continuous)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED						
	Current Dioxin Category Mean[ab]/(n)			Analysis Results for Log_2 (Current Dioxin + 1)		
Model[c]	Low	Medium	High	R^2	Slope (Std. Error)[d]	p-Value
4	57.17 (236)	57.46 (217)	60.02 (214)	0.008	0.0143 (0.0064)	0.025
5	57.12 (242)	57.86 (216)	59.87 (209)	0.009	0.0136 (0.0055)	0.013
6[e]	57.34 (241)	57.85 (216)	59.63 (209)	0.010	0.0117 (0.0059)	0.047

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED							
	Current Dioxin Category Adjusted Mean[a]/(n)			Analysis Results for Log_2 (Current Dioxin + 1)			
Model[c]	Low	Medium	High	R^2	Adj. Slope (Std. Error)[d]	p-Value	Covariate Remarks
4	53.49 (236)	53.88 (217)	56.50 (214)	0.026	0.0147 (0.0073)	0.044	AGE (p=0.014) RACE (p=0.046) OCC (p=0.114) FAST (p=0.692)
5	53.43 (242)	54.23 (216)	56.17 (209)	0.028	0.0138 (0.0062)	0.027	AGE (p=0.015) RACE (p=0.049) OCC (p=0.116) FAST (p=0.684)
6[f]	53.65 (241)	54.27 (216)	56.04 (209)	0.028	0.0123 (0.0067)	0.065	AGE (p=0.017) RACE (p=0.055) OCC (p=0.118) FAST (p=0.687)

[a] Transformed from natural logarithm scale.

[b] Adjusted for fasting status.

[c] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[d] Slope and standard error based on natural logarithm of serum glucagon versus log_2 (current dioxin + 1).

[e] Adjusted for log_2 total lipids.

[f] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 18-47.
Analysis of Serum Glucagon (Nondiabetics)
(Discrete)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Percent Abnormal High
All	***Ranch Hand***	***702***	***0.0***
	Comparison	***944***	***0.0***
Officer	Ranch Hand	265	0.0
	Comparison	376	0.0
Enlisted Flyer	Ranch Hand	124	0.0
	Comparison	154	0.0
Enlisted Groundcrew	Ranch Hand	313	0.0
	Comparison	414	0.0

b) MODEL 2: RANCH HANDS — INITIAL DIOXIN

Initial Dioxin Category Summary Statistics		
Initial Dioxin	n	Percent Abnormal High
Low	122	0.0
Medium	122	0.0
High	122	0.0

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 18-47. (Continued)
Analysis of Serum Glucagon (Nondiabetics)
(Discrete)

c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY		
Dioxin Category	**n**	**Percent Abnormal High**
Comparison	825	0.0
Background RH	298	0.0
Low RH	183	0.0
High RH	186	0.0
Low plus High RH	369	0.0

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

d) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN			
	Current Dioxin Category Percent Abnormal High/(n)		
Model[a]	**Low**	**Medium**	**High**
4	0.0 (236)	0.0 (217)	0.0 (214)
5	0.0 (242)	0.0 (216)	0.0 (209)
6	0.0 (241)	0.0 (216)	0.0 (209)

[a] Model 4: $\log_2$ (lipid-adjusted current dioxin + 1).
Model 5: $\log_2$ (whole-weight current dioxin + 1).
Model 6: $\log_2$ (whole-weight current dioxin + 1), adjusted for $\log_2$ total lipids.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 18-48.
Analysis of α-1-C Hemoglobin (percent) (All Participants) (Continuous)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Mean[a]**	**Difference of Means (95% C.I.)[b]**	**p-Value[c]**
All	*Ranch Hand*	*950*	*7.16*	*0.00 --*	*0.978*
	Comparison	*1,277*	*7.16*		
Officer	Ranch Hand	365	7.09	0.03 --	0.702
	Comparison	502	7.06		
Enlisted Flyer	Ranch Hand	162	7.25	-0.13 --	0.343
	Comparison	202	7.38		
Enlisted Groundcrew	Ranch Hand	423	7.19	0.01 --	0.851
	Comparison	573	7.18		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED						
Occupational Category	**Group**	**n**	**Adj. Mean[a]**	**Difference of Adj. Means (95% C.I.)[b]**	**p-Value[c]**	**Covariate Remarks[d]**
All	*Ranch Hand*	*932*	*7.56*	*0.01 --*	0.873	AGE*RACE (p=0.025)
	Comparison	*1,259*	*7.55*			AGE*BFAT (p=0.020)
Officer	Ranch Hand	359	7.05	0.01 --	0.892	RACE*OCC (p=0.002)
	Comparison	499	7.04			RACE*FAMDIAB (p=0.041)
Enlisted Flyer	Ranch Hand	159	7.87	-0.10 --	0.433	
	Comparison	197	7.97			
Enlisted Groundcrew	Ranch Hand	414	7.73	0.04 --	0.557	
	Comparison	563	7.69			

[a] Transformed from the natural logarithm scale.

[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.

[c] P-values based on difference of means on natural logarithm scale.

[d] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 18-48. (Continued)
Analysis of α-1-C Hemoglobin (percent) (All Participants)
(Continuous)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	173	7.13	7.15	0.070	0.0106 (0.0061)	0.082
Medium	172	7.26	7.29			
High	173	7.36	7.31			

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED						
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[d]			
Initial Dioxin	n	Adj. Mean[ad]	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
Low	171	****	0.195	****	****	INIT*OCC (p=0.009) AGE (p=0.001) BFAT (p=0.025) RACE*OCC (p=0.007) RACE*FAMDIAB (p=0.048) OCC*FAMDIAB (p=0.050)
Medium	167	****				
High	168	****				

[a] Transformed from the natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Slope and standard error based on natural logarithm of α-1-C hemoglobin versus $\log_2$ (initial dioxin).

[d] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

**** Log_2 (initial dioxin)-by-covariate interaction ($p \leq 0.01$); adjusted mean, adjusted slope, standard error, and p-value not presented; refer to Appendix Table N-2-26 for further analysis of this interaction.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 18-48. (Continued)
Analysis of α-1-C Hemoglobin (percent) (All Participants)
(Continuous)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED					
Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,060	7.16	7.16		
Background RH	374	7.05	7.13	-0.02 --	0.725
Low RH	258	7.20	7.16	0.00 --	0.971
High RH	260	7.30	7.23	0.03 --	0.330
Low plus High RH	518	7.25	7.20	0.04 --	0.513

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED					
Dioxin Category	n	Adj. Mean[ae]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]	Covariate Remarks
Comparison	1,045	7.58**			DXCAT*BFAT (p=0.010) AGE*BFAT (p=0.009) RACE*OCC (p<0.001) RACE*FAMDIAB (p=0.018)
Background RH	368	7.57**	-0.01 -- **	0.929**	
Low RH	252	7.53**	-0.05 -- **	0.576**	
High RH	254	7.69**	0.11 -- **	0.185**	
Low plus High RH	506	7.61**	0.03 -- **	0.602**	

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Difference of adjusted means after transformation to original scale; confidence interval on difference of adjusted means not presented because analysis was performed on natural logarithm scale.

[d] P-value is based on difference of means on natural logarithm scale.

[e] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Categorized dioxin-by-covariate interaction ($p \leq 0.05$); adjusted mean, difference of adjusted means, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table N-2-26 for further analysis of this interaction.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤10 ppt.
Background (Ranch Hand): Current Dioxin ≤10 ppt.
Low (Ranch Hand): Current Dioxin >10 ppt, 10 ppt < Initial Dioxin ≤143 ppt.
High (Ranch Hand): Current Dioxin >10 ppt, Initial Dioxin >143 ppt.

Table 18-48. (Continued)
Analysis of α-1-C Hemoglobin (percent) (All Participants) (Continuous)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED						
	Current Dioxin Category Mean[a]/(n)			Analysis Results for Log_2 (Current Dioxin + 1)		
Model[b]	Low	Medium	High	R^2	Slope (Std. Error)[c]	p-Value
4	7.02 (295)	7.19 (299)	7.29 (298)	0.011	0.0123 (0.0038)	0.001
5	7.03 (300)	7.11 (296)	7.37 (296)	0.016	0.0126 (0.0033)	<0.001
6[d]	7.10 (299)	7.12 (296)	7.29 (296)	0.036	0.0072 (0.0035)	0.042

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED							
	Current Dioxin Category Adjusted Mean[a]/(n)			Analysis Results for Log_2 (Current Dioxin + 1)			
Model[b]	Low	Medium	High	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
4	7.47** (290)	7.52** (294)	7.71** (290)	0.106	0.0113 (0.0045)**	0.012**	CURR*BFAT (p=0.022) AGE (p<0.001) FAMDIAB (p<0.001) OCC*RACE (p=0.049)
5	7.48** (296)	7.45** (290)	7.84** (288)	0.132	0.0121 (0.0039)**	0.002**	CURR*AGE (p=0.006) CURR*BFAT (p=0.001) FAMDIAB (p<0.001) AGE*OCC (p=0.022) OCC*RACE (p=0.014)
6[e]	7.58** (295)	7.47** (290)	7.75** (288)	0.147	0.0064 (0.0041)**	0.124**	CURR*AGE (p=0.008) CURR*BFAT (p=0.002) FAMDIAB (p<0.001) AGE*OCC (p=0.021) OCC*RACE (p=0.009)

[a] Transformed from natural logarithm scale.
[b] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.
[c] Slope and standard error based on natural logarithm of α-1-C hemoglobin versus log_2 (current dioxin + 1).
[d] Adjusted for log_2 total lipids.
[e] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted mean, adjusted slope, standard error, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table N-2-26 for further analysis of this interaction.

Note: Model 4: Low = ≤8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤46 ppq; Medium = >46-128 ppq; High = >128 ppq.

the age-by-race, age-by-body fat, race-by-occupation, and race-by-family history of diabetes interactions.

A marginally significant relationship between α-1-C hemoglobin and initial dioxin was disclosed in the Model 2 unadjusted analysis (Table 18-48(c): p=0.082, Slope=0.0106). The adjusted mean α-1-C hemoglobin levels were 7.15 percent, 7.29 percent, and 7.31 percent for the low, medium, and high dioxin categories. In the adjusted analysis, a highly significant interaction between initial dioxin and occupation was revealed (Table 18-48(d): p=0.009). Refer to Appendix Table N-2-26 for further analysis of this interaction. Age, body fat, and the race-by-occupation, race-by-family history of diabetes, and occupation-by-family history of diabetes interactions were retained in the adjusted analysis.

The Model 3 unadjusted analysis did not reveal significant differences between Ranch Hands and Comparisons (Table 18-48(e): p≥0.33). However, in the adjusted analysis, a significant interaction between categorized dioxin and body fat was found (Table 18-48(f): p=0.010). Appendix Table N-2-26 shows stratified results from further analyzing this interaction. No significant differences between Ranch Hands and Comparisons were evident after the interaction was deleted from the final model (p>0.18). However, after occupation and body fat were removed from the final model, a significant difference between high Ranch Hands and Comparisons was revealed (Appendix Table N-3-33: p=0.047). Mean α-1-C hemoglobin for Ranch Hands in the high current dioxin category was 7.76 percent compared to 7.59 percent for Comparisons. The age-by-body fat, race-by-occupation, and race-by-family history of diabetes interactions also were significant in the adjusted analysis.

Each of the Model 4, 5, and 6 unadjusted analyses revealed a significant association between α-1-C hemoglobin and current dioxin, with α-1-C hemoglobin increasing with dioxin (Table 18-48(g): p=0.001, Slope=0.0123 for Model 4; p<0.001, Slope=0.0126 for Model 5; and p=0.042, Slope=0.0072 for Model 6). After adjustment was made for covariates in the Model 4 analysis, the interaction of current dioxin and body fat was significant (Table 18-48(h): p=0.022). Appendix Table N-2-26 presents stratified results from additional analysis of the interaction. After deletion of the interaction from the final model, a significant dioxin effect remained (p=0.012). Adjusted means for the low, medium, and high categories of current dioxin were 7.47, 7.52, and 7.71 percent. Additional covariates retained in the adjusted analysis included age, family history of diabetes, and the occupation-by-race interaction. In the Model 5 adjusted analysis, there were two significant interactions with current dioxin, one involving age and the other involving body fat. Stratified results of this interaction are presented in Appendix Table N-2-26. A highly significant dioxin effect remained after removal of the interactions from the final model (p=0.002). Adjusted means for the low, medium, and high dioxin categories were 7.48, 7.45, and 7.84 percent. Similar results were obtained in the Model 6 adjusted analysis. A three-way interaction involving current dioxin, age, and body fat was significant and included in the final model (p=0.015). Appendix Table N-2-26 displays the stratified results of this interaction. The dioxin effect was nonsignificant after removal of interactions from the final model (p=0.124), but became significant after body fat and occupation also were removed (Appendix Table N-3-33: p=0.002). Additional covariates retained in each of the Model 5 and Model 6 adjusted analyses included family history of diabetes and the age-by-occupation and occupation-by-race interactions.

α-1-C Hemoglobin (All Participants—Discrete)

Neither the unadjusted nor adjusted Model 1 analysis of α-1-C hemoglobin revealed significant results (Table 18-49(a,b): $p>0.24$ for all contrasts). Significant covariates included age, body fat, family history of diabetes, and the occupation-by-race interaction.

The Model 2 unadjusted analysis of α-1-C hemoglobin did not reveal a significant association with initial dioxin (Table 18-49(c): $p=0.773$). However, in the adjusted analysis, a significant interaction between initial dioxin and occupation was disclosed (Table 18-49(d): $p=0.030$). Stratified results from additional analysis on this interaction are presented in Appendix Table N-2-27. A significant association between initial dioxin and α-1-C hemoglobin was not evident after removal of the interaction from the final model ($p=0.300$). Age, race, and family history of diabetes were retained in the adjusted analysis.

Neither the unadjusted nor adjusted Model 3 analyses of α-1-C hemoglobin revealed significant differences between Ranch Hands and Comparisons (Table 18-49(e,f): $p>0.52$ for all analyses). Covariates retained in the adjusted analysis included age, race, occupation, body fat, and family history of diabetes.

In both the Model 4 and 5 unadjusted analyses of α-1-C hemoglobin, a marginally significant or significant association with current dioxin was found (Table 18-49(g): $p=0.071$, Est. RR=1.10 for Model 4 and $p=0.016$, Est. RR=1.11 for Model 5). Adjustment for total lipids in the Model 6 unadjusted analysis led to nonsignificant results ($p=0.352$). After adjusting for age, race, personality type, body fat, and family history of diabetes in the Model 4 analysis, the dioxin effect was no longer significant (Table 18-49(h): $p=0.212$). However, removal of body fat from the final model again caused the dioxin effect to become significant (Appendix Table N-3-34: $p=0.013$, Est. RR=1.15. In the Model 5 adjusted analysis, the interaction of current dioxin and body fat was significant (Table 18-49(g): $p=0.039$). Refer to Appendix Table N-2-27 for further analysis of this interaction. After deletion of the interaction from the final model, a marginally significant dioxin effect remained ($p=0.072$, Est. RR=1.10). The interaction of current dioxin and body fat also was significant in the Model 6 adjusted analysis ($p=0.046$). Results from further analysis of this interaction are shown in Appendix Table N-2-27. The association between current dioxin and α-1-C hemoglobin was not significant once the interaction was removed from the final model ($p=0.713$).

α-1-C Hemoglobin (Diabetics—Continuous)

In the Model 1 unadjusted analysis of α-1-C hemoglobin restricted to diabetics, no significant group differences were revealed (Table 18-50(a): $p>0.62$ for all analyses). However, in the adjusted analysis, a highly significant interaction between group and age was revealed (Table 18-50(b): $p=0.005$). See Appendix Table N-2-28 for additional analysis of the interaction. Significant covariates in the adjusted analysis included race, diabetic severity, and the age-by-occupation and body fat-by-family history of diabetes interactions.

Table 18-49.
Analysis of α-1-C Hemoglobin (All Participants)
(Discrete)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Abnormal High**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***950***	***26.9***	***1.03 (0.85,1.25)***	***0.774***
	Comparison	***1,277***	***26.3***		
Officer	Ranch Hand	365	24.1	1.09 (0.80,1.50)	0.639
	Comparison	502	22.5		
Enlisted Flyer	Ranch Hand	162	30.2	0.78 (0.50,1.22)	0.330
	Comparison	202	35.6		
Enlisted Groundcrew	Ranch Hand	423	28.1	1.09 (0.83,1.45)	0.581
	Comparison	573	26.4		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***1.05 (0.86,1.29)***	***0.626***	AGE ($p<0.001$) BFAT ($p<0.001$) FAMDIAB ($p<0.001$) OCC*RACE ($p=0.005$)
Officer	1.08 (0.77,1.50)	0.660	
Enlisted Flyer	0.75 (0.47,1.22)	0.249	
Enlisted Groundcrew	0.99 (0.73,1.33)	0.934	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 18-49. (Continued)
Analysis of α-1-C Hemoglobin (All Participants)
(Discrete)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Abnormal High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	173	27.7	1.02 (0.88,1.18)	0.773
Medium	172	31.4		
High	173	28.3		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
506	1.10 (0.92,1.32)**	0.300**	INIT*OCC (p=0.030) AGE (p=0.003) RACE (p=0.042) FAMDIAB (p=0.001)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Log_2 (initial dioxin)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table N-2-27 for further analysis of this interaction.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 18-49. (Continued)
Analysis of α-1-C Hemoglobin (All Participants)
(Discrete)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Percent Abnormal High	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,060	26.1		
Background RH	374	23.5	1.02 (0.77,1.35)	0.893
Low RH	258	29.5	1.11 (0.81,1.50)	0.523
High RH	260	28.8	1.01 (0.74,1.38)	0.938
Low plus High RH	518	29.2	1.06 (0.83,1.34)	0.646

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,045			AGE ($p<0.001$) RACE ($p<0.001$) OCC ($p=0.002$) BFAT ($p=0.021$) FAMDIAB ($p<0.001$)
Background RH	368	1.07 (0.79,1.44)	0.675	
Low RH	252	1.02 (0.74,1.41)	0.898	
High RH	254	1.07 (0.77,1.49)	0.699	
Low plus High RH	506	1.04 (0.81,1.34)	0.742	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 18-49. (Continued)
Analysis of α-1-C Hemoglobin (All Participants)
(Discrete)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Abnormal High/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	23.4 (295)	28.4 (299)	28.5 (298)	1.10 (0.99,1.21)	0.071
5	22.0 (300)	28.4 (296)	30.1 (296)	1.11 (1.02,1.22)	0.016
6[c]	22.1 (299)	28.4 (296)	30.1 (296)	1.05 (0.95,1.15)	0.352

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	873	1.08 (0.96,1.21)	0.212	AGE (p<0.001) RACE (p=0.003) PERS (p=0.073) BFAT (p<0.001) FAMDIAB (p<0.001)
5	873	1.10 (0.99,1.21)**	0.072**	CURR*BFAT (p=0.039) AGE (p<0.001) RACE (p=0.003) PERS (p=0.089) FAMDIAB (p=0.001)
6[d]	872	1.02 (0.91,1.14)**	0.713**	CURR*BFAT (p=0.046) AGE (p<0.001) RACE (p=0.001) PERS (p=0.047) FAMDIAB (p=0.001)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.
[b] Relative risk for a twofold increase in current dioxin.
[c] Adjusted for log_2 total lipids.
[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table N-2-27 for further analysis of this interaction.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 18-50.
Analysis of α-1-C Hemoglobin (percent) (Diabetics)
(Continuous)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	*Ranch Hand*	*142*	*9.02*	*0.01 --*	*0.984*
	Comparison	*179*	*9.01*		
Officer	Ranch Hand	55	8.89	-0.03 --	0.943
	Comparison	58	8.92		
Enlisted Flyer	Ranch Hand	25	8.99	-0.34 --	0.635
	Comparison	36	9.33		
Enlisted Groundcrew	Ranch Hand	62	9.15	0.20 --	0.628
	Comparison	85	8.95		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Group	n	Adj. Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]	Covariate Remarks[d]
All	*Ranch Hand*	*137*	****	****	****	GROUP*AGE (p=0.005)
	Comparison	*177*				RACE (p=0.008)
Officer	Ranch Hand	53	****	****	****	DIABSEV (p<0.001)
	Comparison	58				AGE*OCC (p=0.024)
Enlisted Flyer	Ranch Hand	24	****	****	****	BFAT*FAMDIAB (p=0.015)
	Comparison	34				
Enlisted Groundcrew	Ranch Hand	60	****	****	****	
	Comparison	85				

[a] Transformed from the natural logarithm scale.

[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.

[c] P-values based on difference of means on natural logarithm scale.

[d] Covariates and associated p-values correspond to final model based on all participants with available data.

**** Group-by-covariate interaction ($p \leq 0.01$); adjusted mean, difference of adjusted means, and p-value not presented; refer to Appendix Table N-2-28 for further analysis this interaction.

Table 18-50. (Continued)
Analysis of α-1-C Hemoglobin (percent) (Diabetics)
(Continuous)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	31	8.81	8.91	0.113	0.0360 (0.0199)	0.074
Medium	31	8.79	8.87			
High	34	10.22	10.03			

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED						
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[d]			
Initial Dioxin	n	Adj. Mean[ad]	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
Low	31	10.57	0.524	0.0300 (0.0193)	0.124	RACE (p=0.002) BFAT (p=0.027) OCC*DIABSEV (p=0.001)
Medium	31	10.43				
High	34	11.68				

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Slope and standard error based on natural logarithm of α-1-c hemoglobin versus log_2 (initial dioxin).

[d] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 18-50. (Continued)
Analysis of α-1-C Hemoglobin (percent) (Diabetics) (Continuous)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	148	8.90	8.89		
Background RH	42	8.52	8.69	-0.20 --	0.629
Low RH	49	8.82	8.78	-0.11 --	0.778
High RH	47	9.77	9.70	0.81 --	0.053
Low plus High RH	96	9.28	9.22	0.33 --	0.301

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Mean[ae]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]	Covariate Remarks
Comparison	148	10.22			RACE ($p<0.001$) BFAT ($p=0.025$) AGE*OCC ($p=0.008$) OCC*DIABSEV ($p=0.004$)
Background RH	42	10.32	0.10 --	0.822	
Low RH	49	10.02	-0.20 --	0.621	
High RH	47	10.78	0.56 --	0.195	
Low plus High RH	96	10.38	0.16 --	0.605	

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Difference of adjusted means after transformation to original scale; confidence interval on difference of adjusted means not presented because analysis was performed on natural logarithm scale.

[d] P-value is based on difference of means on natural logarithm scale.

[e] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 18-50. (Continued)
Analysis of α-1-C Hemoglobin (percent) (Diabetics) (Continuous)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED						
	Current Dioxin Category Mean[a]/(n)			Analysis Results for Log_2 (Current Dioxin + 1)		
Model[b]	Low	Medium	High	R^2	Slope (Std. Error)[c]	p-Value
4	8.49 (28)	8.81 (56)	9.59 (54)	0.048	0.0391 (0.0149)	0.010
5	8.70 (26)	8.32 (54)	9.93 (58)	0.050	0.0334 (0.0124)	0.008
6[d]	8.89 (26)	8.38 (54)	9.77 (58)	0.064	0.0241 (0.0141)	0.090

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED							
	Current Dioxin Category Adjusted Mean[a]/(n)			Analysis Results for Log_2 (Current Dioxin + 1)			
Model[b]	Low	Medium	High	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
4	10.51 (26)	10.71 (55)	11.21 (52)	0.475	0.0237 (0.0164)	0.152	AGE (p=0.139) RACE (p=0.025) BFAT (p=0.050) OCC*DIABSEV (p=0.005) FAMDIAB*DIABSEV (p=0.018)
5	10.84 (24)	10.23 (53)	11.63 (56)	0.476	0.0196 (0.0134)	0.145	AGE (p=0.139) RACE (p=0.025) BFAT (p=0.057) OCC*DIABSEV (p=0.006) FAMDIAB*DIABSEV (p=0.022)
6[e]	10.92 (24)	10.18 (53)	11.62 (56)	0.468	0.0168 (0.0155)	0.281	RACE (p=0.021) BFAT (p=0.052) OCC*DIABSEV (p=0.008) FAMDIAB*DIABSEV (p=0.038)

[a] Transformed from natural logarithm scale.

[b] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[c] Slope and standard error based on natural logarithm of α-1-C hemoglobin versus log_2 (current dioxin + 1).

[d] Adjusted for log_2 total lipids.

[e] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

In the unadjusted Model 2 analysis, a marginally significant association between initial dioxin and α-1-C hemoglobin restricted to diabetes was revealed (Table 18-50(c): p=0.074, Slope=0.0360). Means for the low and medium categories of initial dioxin were 8.91 and 8.87 percent compared to 10.03 percent for the high category. After adjustment was made for race, body fat, and the occupation-by-diabetic severity interaction, the dioxin effect was no longer significant (Table 18-50(d): p=0.124). However, after body fat and occupation were removed from the adjusted model, the association with dioxin became marginally significant (Appendix Table N-3-35: p=0.092, Slope=0.0313).

In the Model 3 unadjusted analysis, mean α-1-C hemoglobin was marginally greater in diabetic high Ranch Hands (9.70 percent) than in diabetic Comparisons (8.89 percent) (Table 18-50(e): p=0.053, Diff. of Adj. Mean= 0.81). However, in the adjusted analysis, a significant difference between the two groups was not evident. The remaining three contrasts also were nonsignificant in the adjusted analysis (Table 18-50(f): p>0.19). Race, body fat, and the age-by-occupation and occupation-by-diabetic severity interactions were retained in the adjusted model.

In each of the Model 4 through 6 unadjusted analyses, the association between α-1-C hemoglobin and current dioxin in diabetics was significant or marginally significant (Table 18-50(g): p=0.010, Slope=0.0391 for Model 4; p=0.008, Slope=0.0334 for Model 5; and p=0.090, Slope=0.0241 for Model 6). After adjustment was made for covariate information, the dioxin effect was no longer significant in any of the three analyses (Table 18-50(h): p>0.14). However, after the removal of occupation and body fat from the adjusted model, significant and marginally significant positive associations with dioxin were detected for Models 4, 5, and 6 (Table N-3-35): p=0.034, Slope=0.0321 for Model 4; p=0.020, Slope=0.0291 for Model 5; and p=0.059, Slope=0.0259 for Model 6). In the Model 4 and 5 adjusted analyses, significant covariates included age, race, body fat, and the occupation-by-diabetic severity and family history of diabetes-by-diabetic severity interactions. In the Model 6 adjusted analysis, race, body fat, the occupation-by-diabetic severity and family history of diabetes-by-diabetic severity interactions were significant.

α-1-C Hemoglobin (Diabetics—Discrete)

In the Model 1 unadjusted and adjusted analyses restricted to diabetics, the percentage of Ranch Hands with abnormally high α-1-C hemoglobin levels did not differ significantly from that of the Comparisons (Table 18-51(a,b): p>0.27 for all analyses). In the adjusted analysis, significant covariates were age, personality type, occupation, and the body fat-by-diabetic severity and family history of diabetes-by-body fat interactions.

The association between initial dioxin and α-1-C hemoglobin in diabetics was nonsignificant in the Model 2 unadjusted and adjusted analyses (Table 18-51(c,d): p≥0.87). The adjusted analysis retained race and diabetic severity.

In the unadjusted Model 3 analysis, a marginally significant difference in diabetic participants with abnormally high α-1-C hemoglobin was seen for low plus high Ranch Hands versus Comparisons (Table 18-51(e): p=0.096, Est. RR=1.76). However, after adjustment was made for race, diabetic severity, and the age-by-body fat interaction, the difference was

Table 18-51.
Analysis of α-1-C Hemoglobin (Diabetics)
(Discrete)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Abnormal High**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***142***	***79.6***	***1.20 (0.70,2.04)***	***0.605***
	Comparison	***179***	***76.5***		
Officer	Ranch Hand	55	78.2	1.14 (0.47,2.74)	0.945
	Comparison	58	75.9		
Enlisted Flyer	Ranch Hand	25	80.0	0.97 (0.27,3.48)	0.999
	Comparison	36	80.6		
Enlisted Groundcrew	Ranch Hand	62	80.6	1.37 (0.61,3.04)	0.570
	Comparison	85	75.3		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***1.22 (0.65,2.29)***	***0.533***	AGE (p<0.001)
Officer	1.11 (0.37,3.26)	0.855	PERS (p=0.125) OCC (p=0.071)
Enlisted Flyer	0.60 (0.13,2.79)	0.516	BFAT*DIABSEV (p=0.024)
Enlisted Groundcrew	1.76 (0.63,4.90)	0.277	FAMDIAB*BFAT (p=0.014)

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 18-51. (Continued)
Analysis of α-1-C Hemoglobin (Diabetics)
(Discrete)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Abnormal High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	31	87.1	1.02 (0.66,1.57)	0.931
Medium	31	74.2		
High	34	88.2		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
96	1.04 (0.66,1.63)	0.870	RACE (p=0.028) DIABSEV (p=0.005)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 18-51. (Continued)
Analysis of α-1-C Hemoglobin (Diabetics)
(Discrete)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	**n**	**Percent Abnormal High**	**Est. Relative Risk (95% C.I.)[ab]**	**p-Value**
Comparison	148	73.6		
Background RH	42	69.0	1.11 (0.50,2.45)	0.798
Low RH	49	81.6	1.59 (0.69,3.65)	0.273
High RH	47	85.1	1.97 (0.80,4.85)	0.140
Low plus High RH	96	83.3	1.76 (0.90,3.42)	0.096

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	**n**	**Adj. Relative Risk (95% C.I.)[ac]**	**p-Value**	**Covariate Remarks**
Comparison	148			AGE*BFAT (p=0.014) RACE (p=0.017) DIABSEV (p<0.001)
Background RH	42	0.96 (0.40,2.32)	0.935	
Low RH	49	1.52 (0.61,3.84)	0.371	
High RH	47	2.16 (0.81,5.78)	0.126	
Low plus High RH	96	1.80 (0.87,3.72)	0.113	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 18-51. (Continued)
Analysis of α-1-C Hemoglobin (Diabetics)
(Discrete)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Abnormal High/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	71.4 (28)	78.6 (56)	83.3 (54)	1.23 (0.92,1.64)	0.142
5	65.4 (26)	77.8 (54)	86.2 (58)	1.20 (0.95,1.51)	0.116
6[c]	65.4 (26)	77.8 (54)	86.2 (58)	1.09 (0.84,1.42)	0.512

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	138	1.41 (0.96,2.09)	0.070	AGE (p=0.011) RACE (p=0.124) BFAT (p=0.015) DIABSEV (p<0.001)
5	138	1.42 (1.01,2.02)	0.035	AGE*RACE (p=0.045) BFAT (p=0.030) DIABSEV (p<0.001)
6[d]	138	1.24 (0.84,1.83)	0.267	AGE*RACE (p=0.025) BFAT (p=0.039) DIABSEV (p<0.001)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

no longer significant (Table 18-51(f): p=0.113). The other contrasts examining differences between Ranch Hands and Comparisons were nonsignificant as well (p>0.12 for the remaining contrasts).

Although the Model 4 unadjusted analysis did not reveal a significant association between current dioxin and α-1-C hemoglobin in diabetics, adjustment for age, race, body fat, and diabetic severity led to a marginally significant positive dioxin effect (Table 18-51(g,h): p=0.142 for the unadjusted analysis; p=0.070, Adj. RR=1.41 for the adjusted analysis). Similarly, the Model 5 unadjusted analysis revealed no significant findings; however, adjusting for covariate information revealed a significant association between current dioxin and α-1-C hemoglobin in diabetics (p=0.116 for the unadjusted analysis; p=0.035, Adj. RR=1.42 for the adjusted analysis). Significant covariates included body fat, diabetic severity, and the age-by-race interaction. Neither the unadjusted nor the adjusted Model 6 analyses disclosed any significant results (p>0.26). Covariates significant in the adjusted analysis were body fat, diabetic severity, and the age-by-race interaction.

α-1-C Hemoglobin (Nondiabetics—Continuous)

Nondiabetic Ranch Hands and Comparisons did not have significantly different mean levels of α-1-C hemoglobin in the unadjusted Model 1 analysis (Table 18-52(a): p>0.37 for all contrasts). In the adjusted analysis, the interaction of group and body fat was significant (Table 18-52(b): p=0.036). The interaction was further analyzed, and results are presented in Appendix Table N-2-29. After removal of the interaction from the final model, no significant differences between Ranch Hands and Comparisons were evident (p>0.28 for all analyses). Additional significant covariates in the adjusted analysis included race, occupation, and the age-by-family history of diabetes interaction.

Restricted to nondiabetics, the Model 2 analyses of α-1-C hemoglobin disclosed no significant results (Table 18-52(c,d): p>0.83). Retained in the adjusted analysis were age and the occupation-by-family history of diabetes and the body fat-by-race interactions.

Two marginally significant negative differences between Ranch Hands and Comparisons were revealed in the Model 3 unadjusted analysis of α-1-C hemoglobin in nondiabetics. Both high Ranch Hands and low plus high Ranch Hands had significantly lower mean levels of α-1-C hemoglobin than Comparisons (Table 18-52(e): p=0.095 for high Ranch Hands vs. Comparisons and p=0.091 for low plus high Ranch Hands vs. Comparisons). The α-1-C hemoglobin means were 6.83 percent and 6.85 percent for high and low plus high Ranch Hands respectively, compared to 6.91 percent for Comparisons. After adjustment was made for age, race, occupation, body fat, and family history of diabetes, only the difference between low plus high Ranch Hands and Comparisons remained marginally significant (Table 18-52(f): p=0.053, Diff. of Adj. Mean=-0.07. For this Ranch Hand category, the adjusted α-1-C hemoglobin mean was 7.05 percent versus 7.12 percent for Comparisons. Removal of occupation and body fat from the final model caused the difference between low plus high Ranch Hands and Comparisons to become nonsignificant (Appendix Table N-3-37: p=0.179).

None of the Model 4 through 6 unadjusted analyses restricted to nondiabetics revealed any significant associations between α-1-C hemoglobin and current dioxin (Table 18-52(g):

Table 18-52.
Analysis of α-1-C Hemoglobin (percent) (Nondiabetics) (Continuous)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	*Ranch Hand*	*808*	*6.88*	*-0.02 --*	*0.431*
	Comparison	*1,098*	*6.90*		
Officer	Ranch Hand	310	6.81	-0.04 --	0.375
	Comparison	444	6.85		
Enlisted Flyer	Ranch Hand	137	6.96	-0.05 --	0.563
	Comparison	166	7.01		
Enlisted Groundcrew	Ranch Hand	361	6.90	0.00 --	0.871
	Comparison	488	6.90		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Group	n	Adj. Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]	Covariate Remarks[d]
All	*Ranch Hand*	*795*	*7.07***	*-0.02 -- ***	*0.381***	GROUP*BFAT (p=0.036)
	Comparison	*1,082*	*7.09***			RACE (p<0.001)
Officer	Ranch Hand	306	6.96**	-0.05 -- **	0.288**	OCC (p<0.001)
	Comparison	441	7.01**			AGE*FAMDIAB (p=0.034)
Enlisted Flyer	Ranch Hand	135	7.13**	-0.04 -- **	0.558**	
	Comparison	163	7.17**			
Enlisted Groundcrew	Ranch Hand	354	7.11**	0.00 -- **	0.967**	
	Comparison	478	7.11**			

[a] Transformed from the natural logarithm scale.

[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.

[c] P-values based on difference of means on natural logarithm scale.

[d] Covariates and associated p-values correspond to final model based on all participants with available data.

** Group-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted mean, difference of adjusted means, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table N-2-29 for further analysis of this interaction.

Table 18-52. (Continued)
Analysis of α-1-C Hemoglobin (percent) (Nondiabetics) (Continuous)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	142	6.81	6.81	0.008	-0.0001 (0.0032)	0.984
Medium	141	6.96	6.97			
High	139	6.79	6.78			

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED						
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[d]			
Initial Dioxin	n	Adj. Mean[ad]	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
Low	140	6.89	0.105	0.0007 (0.0036)	0.837	AGE (p<0.001) OCC*FAMDIAB (p=0.009) BFAT*RACE (p=0.032)
Medium	137	7.06				
High	135	6.91				

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Slope and standard error based on natural logarithm of α-1-C hemoglobin versus $\log_2$ (initial dioxin).

[d] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 18-52. (Continued)
Analysis of α-1-C Hemoglobin (percent) (Nondiabetics) (Continuous)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED					
Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	912	6.91	6.91		
Background RH	332	6.89	6.89	-0.02 --	0.742
Low RH	209	6.86	6.86	-0.05 --	0.350
High RH	213	6.84	6.83	-0.08 --	0.095
Low plus High RH	422	6.85	6.85	-0.06 --	0.091

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED					
Dioxin Category	n	Adj. Mean[ae]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]	Covariate Remarks
Comparison	898	7.12			AGE ($p<0.001$) RACE ($p<0.001$) OCC ($p=0.002$) BFAT ($p<0.001$) FAMDIAB ($p=0.005$)
Background RH	329	7.12	0.00 --	0.902	
Low RH	204	7.05	-0.07 --	0.132	
High RH	208	7.05	-0.07 --	0.142	
Low plus High RH	412	7.05	-0.07 --	0.053	

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Difference of adjusted means after transformation to original scale; confidence interval on difference of adjusted means not presented because analysis was performed on natural logarithm scale.

[d] P-value is based on difference of means on natural logarithm scale.

[e] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 18-52. (Continued)
Analysis of α-1-C Hemoglobin (percent) (Nondiabetics)
(Continuous)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED						
	Current Dioxin Category Mean[a]/(n)			Analysis Results for Log_2 (Current Dioxin + 1)		
Model[b]	Low	Medium	High	R^2	Slope (Std. Error)[c]	p-Value
4	6.88 (267)	6.86 (243)	6.86 (244)	<0.001	-0.0011 (0.0023)	0.625
5	6.89 (274)	6.86 (242)	6.85 (238)	<0.001	-0.0002 (0.0020)	0.926
6[d]	6.90 (273)	6.86 (242)	6.84 (238)	0.005	-0.0015 (0.0021)	0.457

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED							
	Current Dioxin Category Adjusted Mean[a]/(n)			Analysis Results for Log_2 (Current Dioxin + 1)			
Model[b]	Low	Medium	High	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
4	7.08** (264)	7.00** (239)	6.98** (238)	0.057	-0.0037 (0.0027)**	0.174**	CURR*RACE (p=0.045) AGE (p<0.001) OCC (p=0.009) FAMDIAB (p=0.005) BFAT*RACE (p=0.037)
5	7.06 (272)	7.00 (237)	6.97 (232)	0.047	-0.0014 (0.0022)	0.519	AGE (p<0.001) RACE (p=0.044) OCC (p=0.012) FAMDIAB (p=0.008)
6[e]	7.09 (271)	7.00 (237)	6.96 (232)	0.050	-0.0028 (0.0024)	0.233	AGE (p<0.001) RACE (p=0.035) OCC (p=0.009) FAMDIAB (p=0.008)

[a] Transformed from natural logarithm scale.
[b] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.
[c] Slope and standard error based on natural logarithm of α-1-C hemoglobin versus log_2 (current dioxin + 1).
[d] Adjusted for log_2 total lipids.
[e] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted mean, adjusted slope, standard error, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table N-2-29 for further analysis of this interaction.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

p>0.45 for all analyses). In the Model 4 adjusted analysis, however, a significant interaction between current dioxin and race was disclosed (Table 18-52(h): p=0.045). Appendix Table N-2-29 presents stratified results from additional analysis on the interaction. After the interaction was removed from the final model, no significant dioxin effect was revealed (p=0.174). Likewise, both the Model 5 and Model 6 adjusted analyses led to nonsignificant results (p>0.23 for both analyses). The Model 4 analysis retained age, occupation, family history of diabetes, and the body fat-by-race interaction, whereas both the Model 5 and Model 6 adjusted analyses retained age, occupation, race, and family history of diabetes.

α-1-C Hemoglobin (Nondiabetics—Discrete)

Neither the Model 1 unadjusted nor adjusted analysis of α-1-C hemoglobin revealed any significant differences between nondiabetic Ranch Hands and Comparisons (Table 18-53(a,b): p>0.32 for all analyses). Significant covariates included age, race, occupation, body fat, and family history of diabetes.

Restricted to nondiabetics, no significant associations between α-1-C hemoglobin and dioxin were disclosed in the Model 2 and Model 3 analyses (Table 18-53(c-f): p>0.25 for all analyses). The Model 2 adjusted analysis retained family history of diabetes and the race-by-body fat interaction, whereas the Model 3 analysis retained age, race, occupation, body fat, and family history of diabetes.

Current dioxin was not significantly associated with α-1-C hemoglobin in any of the Model 4 through 6 analyses restricted to nondiabetics (Table 18-53(g,h): p>0.20 for all analyses). In each of the adjusted analyses, race, personality type, body fat, and family history of diabetes were significant.

Urinary Protein (Diabetics Only)

All contrasts examined from both unadjusted and adjusted Model 1 analyses of urinary protein restricted to diabetics did not indicate significant differences between Ranch Hands and Comparisons (Table 18-54(a,b): p>0.32 for each contrast). Group-by-race was a significant interaction in Model 1. Adjusted relative risks, 95 percent confidence intervals, and p-values were based on the final model after deletion of the group interaction. Results stratified by race are presented in Table N-2-30. Occupation, diabetic severity, and the age-by-family history of diabetes interaction also were significant in the final adjusted model.

Similar to Model 1, results from Models 2 and 3 were nonsignificant for all unadjusted and adjusted analyses of urinary protein in diabetics (Table 18-54(c-f): p>0.12 for all analyses). Model 2 adjusted analysis reflects adjustment for diabetic severity only, whereas diabetic severity and the age-by-family history of diabetes interaction were significant in the Model 3 final adjusted model.

All unadjusted and adjusted analyses of Models 4, 5, and 6 displayed nonsignificant associations between current dioxin and presence of urinary protein restricted to diabetics (Table 18-54(g,h): p>0.48 for all analyses). Each model adjusted for the significant covariate effects of race and diabetic severity.

Table 18-53.
Analysis of α-1-C Hemoglobin (Nondiabetics) (Discrete)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Percent Abnormal High	Est. Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*808*	*17.7*	*0.97 (0.77,1.23)*	*0.858*
	Comparison	*1,098*	*18.1*		
Officer	Ranch Hand	310	14.5	0.92 (0.61,1.39)	0.777
	Comparison	444	15.5		
Enlisted Flyer	Ranch Hand	137	21.2	0.77 (0.45,1.31)	0.407
	Comparison	166	25.9		
Enlisted Groundcrew	Ranch Hand	361	19.1	1.09 (0.77,1.55)	0.698
	Comparison	488	17.8		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks[a]
All	*0.98 (0.77,1.25)*	*0.850*	AGE ($p<0.001$)
Officer	0.93 (0.61,1.40)	0.712	RACE ($p<0.001$) OCC ($p=0.003$)
Enlisted Flyer	0.76 (0.44,1.32)	0.328	BFAT ($p<0.001$)
Enlisted Groundcrew	1.13 (0.79,1.62)	0.489	FAMDIAB ($p=0.086$)

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 18-53. (Continued)
Analysis of α-1-C Hemoglobin (Nondiabetics)
(Discrete)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Abnormal High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	142	14.8	1.02 (0.83,1.24)	0.866
Medium	141	22.0		
High	139	13.7		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED

Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
412	1.00 (0.82,1.23)	0.996	FAMDIAB (p=0.028) RACE*BFAT (p=0.012)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 18-53. (Continued)
Analysis of α-1-C Hemoglobin (Nondiabetics)
(Discrete)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Abnormal High	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	912	18.4		
Background RH	332	17.8	1.01 (0.73,1.41)	0.934
Low RH	209	17.2	0.91 (0.61,1.35)	0.631
High RH	213	16.4	0.82 (0.55,1.22)	0.324
Low plus High RH	422	16.8	0.86 (0.63,1.17)	0.338

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	898			AGE ($p<0.001$) RACE ($p<0.001$) OCC ($p=0.003$) BFAT ($p=0.003$) FAMDIAB ($p=0.051$)
Background RH	329	1.10 (0.78,1.56)	0.580	
Low RH	204	0.84 (0.56,1.26)	0.395	
High RH	208	0.82 (0.54,1.26)	0.372	
Low plus High RH	412	0.83 (0.60,1.14)	0.255	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 18-53. (Continued)
Analysis of α-1-C Hemoglobin (Nondiabetics)
(Discrete)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Abnormal High/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	18.4 (267)	16.9 (243)	16.4 (244)	0.99 (0.86,1.12)	0.824
5	17.9 (274)	17.4 (242)	16.4 (238)	1.01 (0.90,1.13)	0.921
6[c]	17.9 (273)	17.4 (242)	16.4 (238)	0.97 (0.86,1.10)	0.648

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	740	0.93 (0.81,1.07)	0.307	RACE (p=0.045) PERS (p=0.121) BFAT (p=0.035) FAMDIAB (p=0.020)
5	740	0.96 (0.85,1.09)	0.525	RACE (p=0.046) PERS (0=0.132) BFAT (p=0.046) FAMDIAB (p=0.022)
6[d]	739	0.92 (0.81,1.05)	0.206	RACE (p=0.030) PERS (p=0.094) BFAT (p=0.040) FAMDIAB (p=0.021)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 18-54.
Analysis of Urinary Protein (Diabetics)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	Group	n	Percent Present	Est. Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*142*	*12.7*	*0.81 (0.43,1.54)*	*0.635*
	Comparison	*178*	*15.2*		
Officer	Ranch Hand	55	12.7	1.06 (0.35,3.25)	0.999
	Comparison	58	12.1		
Enlisted Flyer	Ranch Hand	25	12.0	1.09 (0.22,5.36)	0.999
	Comparison	36	11.1		
Enlisted Groundcrew	Ranch Hand	62	12.9	0.63 (0.25,1.58)	0.445
	Comparison	84	19.1		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks[a]
All	*0.84 (0.42,1.69)***	*0.618***	GROUP*RACE (p=0.026)
Officer	1.04 (0.31,3.48)**	0.945**	OCC (p=0.086)
Enlisted Flyer	1.50 (0.26,8.84)**	0.651**	DIABSEV (p=0.005)
Enlisted Groundcrew	0.61 (0.23,1.63)**	0.323**	AGE*FAMDIAB (p=0.042)

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

** Group-by-covariate interaction ($0.01<p\leq0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table N-2-30 for further analysis of this interaction.

Table 18-54. (Continued)
Analysis of Urinary Protein (Diabetics)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Present	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	31	6.5	1.21 (0.78,1.88)	0.401
Medium	31	9.7		
High	34	14.7		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
96	1.13 (0.72,1.79)	0.586	DIABSEV (p=0.248)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 18-54. (Continued)
Analysis of Urinary Protein (Diabetics)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Present	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	147	16.3		
Background RH	42	16.7	1.26 (0.49,3.28)	0.631
Low RH	49	8.2	0.44 (0.14,1.36)	0.151
High RH	47	12.8	0.68 (0.26,1.83)	0.447
Low plus High RH	96	10.4	0.56 (0.25,1.24)	0.152

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	146			DIABSEV (p=0.026) AGE*FAMDIAB (p=0.025)
Background RH	39	1.48 (0.52,4.23)	0.463	
Low RH	48	0.39 (0.12,1.30)	0.125	
High RH	46	0.80 (0.28,2.28)	0.676	
Low plus High RH	94	0.57 (0.25,1.32)	0.190	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 18-54. (Continued)
Analysis of Urinary Protein (Diabetics)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Present/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	10.7 (28)	14.3 (56)	11.1 (54)	1.11 (0.80,1.53)	0.538
5	11.5 (26)	11.1 (54)	13.8 (58)	1.10 (0.83,1.46)	0.486
6[c]	11.5 (26)	11.1 (54)	13.8 (58)	1.08 (0.79,1.48)	0.619

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	138	1.01 (0.71,1.44)	0.947	RACE (p=0.087) DIABSEV (p=0.061)
5	138	1.02 (0.77,1.37)	0.878	RACE (p=0.090) DIABSEV (p=0.063)
6[d]	138	1.04 (0.75,1.44)	0.826	RACE (p=0.088) DIABSEV (p=0.062)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Serum Proinsulin (Continuous)

Continuous analyses of serum proinsulin were nonsignificant for Models 1, 2, 3, 4, and 6 for all unadjusted and adjusted models (Table 18-55(a-h) $p>0.11$ for each analysis). Race, personality type, fasting status, and the body fat-by-diabetic severity and family history of diabetes-by-diabetic severity interactions were significant in the adjusted analyses of Model 1. Models 2, 4, 5, and 6 adjusted for personality type, body fat, fasting status, and diabetic severity. Model 3 adjusted for race, personality type, and the body fat-by-diabetic severity and family history of diabetes-by-diabetic severity interactions.

The Model 5 unadjusted analysis revealed a significant positive association between serum proinsulin and current dioxin (Table 18-55(g): $p=0.047$, Slope=0.033). Results were nonsignificant after adjustment for the covariate effects of personality type, body fat, fasting status, and diabetic severity (Table 18-55(h): $p=0.529$).

Serum Proinsulin (Discrete)

All unadjusted and adjusted results from the analysis of discrete serum proinsulin were nonsignificant for Models 1, 2, and 3 (Table 18-56(a-f): $p>0.20$ for each analysis). Race and diabetic severity were significant covariates in Models 1 and 3. Age, diabetic severity, and the occupation-by-body fat interaction were significant in Model 2.

Unadjusted analysis for Model 4 revealed a marginally significant association between current dioxin and discrete serum proinsulin (Table 18-56(g): $p=0.077$, Est. RR=1.23). Model 5 unadjusted results displayed a significant association between current dioxin and discrete serum proinsulin (Table 18-56(g): $p=0.031$, Est. RR=1.24). Unadjusted results were nonsignificant for Model 6 (Table 18-56(g): $p=0.359$). Adjusted analyses for Models 4, 5, and 6 each adjusted for the interaction of current dioxin and occupation (Table 18-56 (h): $p=0.001$ for Model 4, $p<0.001$ for Models 5 and 6). Results stratified by occupation are presented in Table N-2-31. Other significant covariates present in the Model 4 final model are diabetic severity, and the age-by-occupation, race-by-body fat, and family history of diabetes-by-body fat interactions. Significant covariates included in Model 5 are body fat, diabetic severity, and the age-by-occupation interaction. Race and current dioxin-by-diabetic severity, age-by-occupation, and personality-by-body fat interactions also were significant in Model 6. See Table N-2-31 for Model 6 results stratified by diabetic severity. Exclusion of body fat and occupation led to a significant association with current dioxin for Ranch Hands who do not receive any treatment for their diabetes (Appendix Table N-4-13: $p=0.037$, Adj. RR=1.60). Additionally, the adjusted relative risks for the diet only and oral hypoglycemic categories became nonsignificant when body fat and occupation were removed (Appendix Table N-4-13: $p=0.298$, and $p=0.246$ respectively).

Serum C Peptide (Continuous)

Each contrast from the Model 1 unadjusted analysis of continuous serum C peptide revealed nonsignificant differences between Ranch Hands and Comparisons (Table 18-57(a): $p\geq0.18$ for each contrast). After adjustment for race, body fat, diabetic severity, and fasting status, the overall and enlisted groundcrew strata contrasts were marginally significant (Table

Table 18-55.
Analysis of Serum Proinsulin (ng/ml) (Diabetics) (Continuous)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Mean[ab]	Difference of Means (95% C.I.)[c]	p-Value[d]
All	***Ranch Hand***	***134***	***0.777***	***-0.044 --***	***0.634***
	Comparison	***173***	***0.820***		
Officer	Ranch Hand	52	0.752	-0.234 --	0.142
	Comparison	57	0.986		
Enlisted Flyer	Ranch Hand	23	0.691	0.024 --	0.902
	Comparison	35	0.667		
Enlisted Groundcrew	Ranch Hand	59	0.833	0.054 --	0.694
	Comparison	81	0.779		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Group	n	Adj. Mean[a]	Difference of Adj. Means (95% C.I.)[c]	p-Value[d]	Covariate Remarks[e]
All	***Ranch Hand***	***129***	***0.809***	***0.023 --***	***0.790***	RACE (p=0.020)
	Comparison	***172***	***0.785***			PERS (p=0.050)
Officer	Ranch Hand	50	0.757	-0.099 --	0.507	FAST (p<0.001)
	Comparison	57	0.856			BFAT*DIABSEV (p<0.001)
Enlisted Flyer	Ranch Hand	22	0.792	0.113 --	0.738	FAMDIAB*DIABSEV (p=0.004)
	Comparison	34	0.679			
Enlisted Groundcrew	Ranch Hand	57	0.871	0.077 --	0.738	
	Comparison	81	0.794			

[a] Transformed from the square root scale.

[b] Adjusted for fasting status.

[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.

[d] P-values based on difference of means on square root scale.

[e] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 18-55. (Continued)
Analysis of Serum Proinsulin (ng/ml) (Diabetics)
(Continuous)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[c]		
Initial Dioxin	n	Mean[ab]	Adj. Mean[ac]	R^2	Slope (Std. Error)[d]	p-Value
Low	29	0.708	0.741	0.426	0.007 (0.025)	0.764
Medium	29	0.878	0.930			
High	33	0.650	0.852			

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED						
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[d]			
Initial Dioxin	n	Adj. Mean[ae]	R^2	Adj. Slope (Std. Error)[d]	p-Value	Covariate Remarks
Low	29	0.754	0.490	-0.003 (0.025)	0.891	PERS (p=0.089)
Medium	29	0.952				BFAT (p=0.129) DIABSEV (p=0.246)
High	33	0.838				FAST (p<0.001)

[a] Transformed from square root scale.

[b] Adjusted for fasting status.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and fasting status.

[d] Slope and standard error based on square root of serum proinsulin versus $\log_2$ (initial dioxin).

[e] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 18-55. (Continued)
Analysis of Serum Proinsulin (ng/ml) (Diabetics)
(Continuous)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Mean[ab]	Adj. Mean[ac]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[d]	p-Value[e]
Comparison	143	0.859	0.847		
Background RH	39	0.624	0.690	-0.157 --	0.278
Low RH	46	0.791	0.794	-0.053 --	0.699
High RH	45	0.847	0.822	-0.024 --	0.862
Low plus High RH	91	0.819	0.808	-0.039 --	0.722

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Mean[af]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[d]	p-Value[e]	Covariate Remarks
Comparison	143	0.738			RACE (p=0.003) PERS (p=0.026) BFAT*DIABSEV (p<0.001) FAMDIAB*DIABSEV (p=0.007)
Background RH	36	0.689	-0.049 --	0.723	
Low RH	45	0.692	-0.046 --	0.709	
High RH	44	0.790	0.052 --	0.688	
Low plus High RH	89	0.740	0.001 --	0.988	

[a] Transformed from square root scale.

[b] Adjusted for fasting status.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and fasting status.

[d] Difference of adjusted means after transformation to original scale; confidence interval on difference of adjusted means not presented because analysis was performed on square root scale.

[e] P-value is based on difference of means on square root scale.

[f] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 18-55. (Continued)
Analysis of Serum Proinsulin (ng/ml) (Diabetics)
(Continuous)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED						
	Current Dioxin Category Mean[ab]/(n)			Analysis Results for Log_2 (Current Dioxin + 1)		
Model[c]	Low	Medium	High	R^2	Slope (Std. Error)[d]	p-Value
4	0.604 (26)	0.712 (52)	0.930 (52)	0.363	0.032 (0.020)	0.113
5	0.558 (24)	0.720 (50)	0.927 (56)	0.370	0.033 (0.016)	0.047
6[e]	0.605 (24)	0.736 (50)	0.888 (56)	0.382	0.020 (0.018)	0.288

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED							
	Current Dioxin Category Adjusted Mean[a]/(n)			Analysis Results for Log_2 (Current Dioxin + 1)			
Model[c]	Low	Medium	High	R^2	Adj. Slope (Std. Error)[d]	p-Value	Covariate Remarks
4	0.717 (26)	0.785 (52)	0.893 (52)	0.463	0.004 (0.021)	0.854	PERS (p=0.035) BFAT (p<0.001) FAST (p<0.001) DIABSEV (p=0.178)
5	0.671 (24)	0.772 (50)	0.912 (56)	0.464	0.011 (0.017)	0.529	PERS (p=0.034) BFAT (p=0.001) FAST (p<0.001) DIABSEV (p=0.213)
6[f]	0.719 (24)	0.787 (50)	0.867 (56)	0.479	-0.006 (0.019)	0.775	PERS (p=0.023) BFAT (p=0.001) FAST (p<0.001) DIABSEV (p=0.176)

[a] Transformed from square root scale.

[b] Adjusted for fasting status.

[c] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[d] Slope and standard error based on square root of serum proinsulin versus log_2 (current dioxin + 1).

[e] Adjusted for log_2 total lipids.

[f] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 18-56.
Analysis of Serum Proinsulin (Diabetics)
(Discrete)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Percent Abnormal High	Est. Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*134*	*41.0*	*0.93 (0.59,1.47)*	*0.851*
	Comparison	*173*	*42.8*		
Officer	Ranch Hand	52	36.5	0.74 (0.34,1.59)	0.560
	Comparison	57	43.9		
Enlisted Flyer	Ranch Hand	23	39.1	0.86 (0.29,2.50)	0.993
	Comparison	35	42.9		
Enlisted Groundcrew	Ranch Hand	59	45.8	1.17 (0.59,2.29)	0.784
	Comparison	81	42.0		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks[a]
All	*0.79 (0.47,1.33)*	*0.368*	RACE (p=0.065) DIABSEV (p<0.001)
Officer	0.78 (0.33,1.89)	0.588	
Enlisted Flyer	0.45 (0.13,1.55)	0.204	
Enlisted Groundcrew	1.03 (0.48,2.21)	0.938	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 18-56. (Continued)
Analysis of Serum Proinsulin (Diabetics)
(Discrete)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Abnormal High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	29	31.0	1.09 (0.81,1.46)	0.556
Medium	29	55.2		
High	33	51.5		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
91	1.26 (0.79,1.99)	0.317	AGE (p=0.116) DIABSEV (p=0.106) OCC*BFAT (p=0.016)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 18-56. (Continued)
Analysis of Serum Proinsulin (Diabetics)
(Discrete)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Abnormal High	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	143	44.1		
Background RH	39	28.2	0.61 (0.27,1.35)	0.219
Low RH	46	43.5	0.99 (0.50,1.95)	0.965
High RH	45	48.9	1.17 (0.59,2.32)	0.656
Low plus High RH	91	46.2	1.07 (0.63,1.84)	0.800

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	143			RACE (p=0.023) DIABSEV (p<0.001)
Background RH	39	0.57 (0.24,1.40)	0.221	
Low RH	46	0.99 (0.46,2.12)	0.979	
High RH	45	0.82 (0.36,1.83)	0.617	
Low plus High RH	91	0.91 (0.49,1.68)	0.749	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 18-56. (Continued)
Analysis of Serum Proinsulin (Diabetics)
(Discrete)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Abnormal High/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	26.9 (26)	36.5 (52)	51.9 (52)	1.23 (0.97,1.55)	0.077
5	25.0 (24)	32.0 (50)	55.4 (56)	1.24 (1.01,1.52)	0.031
6[c]	25.0 (24)	32.0 (50)	55.4 (56)	1.11 (0.88,1.40)	0.359

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	125	****	****	CURR*OCC (p=0.001) DIABSEV (p=0.003) AGE*OCC (p=0.008) RACE*BFAT (p=0.019) FAMDIAB*BFAT (p=0.006)
5	130	****	****	CURR*OCC (p<0.001) BFAT (p=0.066) DIABSEV (p=0.006) AGE*OCC (p=0.002)
6[d]	130	****	****	CURR*OCC (p<0.001) CURR*DIABSEV (p=0.041) RACE (p=0.075) AGE*OCC (p<0.001) PERS*BFAT (p=0.049)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

**** Log_2 (current dioxin + 1)-by-covariate interaction ($p \leq 0.01$); adjusted relative risk, confidence interval, and p-value not presented; refer to Appendix Table N-2-31 for further analysis of this interaction.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 18-57.
Analysis of Serum C Peptide (ng/ml) (Diabetics)
(Continuous)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)	p-Value
All	*Ranch Hand*	*134*	*9.39*	*0.68 (-0.31,1.67)*	*0.180*
	Comparison	*173*	*8.71*		
Officer	Ranch Hand	52	9.32	0.31 (-1.35,1.97)	0.712
	Comparison	57	9.01		
Enlisted Flyer	Ranch Hand	23	8.83	0.76 (-1.57,3.08)	0.523
	Comparison	35	8.07		
Enlisted Groundcrew	Ranch Hand	59	9.66	0.89 (-0.59,2.37)	0.237
	Comparison	81	8.77		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Group	n	Adj. Mean	Difference of Adj. Mean (95% C.I.)	p-Value	Covariate Remarks[b]
All	*Ranch Hand*	*134*	*7.57*	*0.85 (-0.09,1.78)*	*0.077*	RACE (p<0.001)
	Comparison	*173*	*6.72*			BFAT (p<0.001)
Officer	Ranch Hand	52	7.36	0.42 (-1.16,1.20)	0.604	DIABSEV (p=0.007)
	Comparison	57	6.94			FAST (p<0.001)
Enlisted Flyer	Ranch Hand	23	7.39	0.78 (-1.41,2.98)	0.484	
	Comparison	35	6.61			
Enlisted Groundcrew	Ranch Hand	59	7.84	1.20 (-0.19,2.60)	0.092	
	Comparison	81	6.64			

[a] Adjusted for fasting status.

[b] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 18-57. (Continued)
Analysis of Serum C Peptide (ng/ml) (Diabetics)
(Continuous)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[b]	R^2	Slope (Std. Error)	p-Value
Low	29	10.25	10.33	0.636	-0.469 (0.309)	0.133
Medium	29	10.06	9.94			
High	33	9.15	9.06			

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED						
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[c]			
Initial Dioxin	n	Adj. Mean[c]	R^2	Adj. Slope (Std. Error)	p-Value	Covariate Remarks
Low	29	8.36	0.673	-0.569 (0.309)	0.069	RACE (p=0.044) DIABSEV (p=0.128) FAST (p<0.001)
Medium	29	8.42				
High	33	6.91				

[a] Adjusted for fasting status.

[b] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and fasting status.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 18-57. (Continued)
Analysis of Serum C Peptide (ng/ml) (Diabetics)
(Continuous)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Mean[a]	Adj. Mean[b]	Difference of Adj. Mean vs. Comparisons (95% C.I.)	p-Value
Comparison	143	8.68	8.62		
Background RH	39	8.40	8.66	0.04 (-1.55,1.63)	0.962
Low RH	46	10.36	10.40	1.78 (0.32,3.23)	0.017
High RH	45	9.03	8.95	0.32 (-1.15,1.80)	0.668
Low plus High RH	91	9.70	9.68	1.06 (-0.10,2.21)	0.073

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Mean[c]	Difference of Adj. Mean vs. Comparisons (95% C.I.)	p-Value	Covariate Remarks
Comparison	143	6.34**			DXCAT*OCC (p=0.023) RACE (p<0.001) BFAT (p=0.044) FAMDIAB (p=0.078) DIABSEV (p=0.031) FAST (p<0.001)
Background RH	36	6.28**	-0.05 (-1.69,1.58)**	0.948**	
Low RH	45	8.28**	1.94 (0.53,3.37)**	0.008**	
High RH	44	6.75**	0.42 (-1.06,1.90)**	0.579**	
Low plus High RH	89	7.53**	1.19 (0.07,2.31)**	0.038**	

[a] Adjusted for fasting status.

[b] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and fasting status.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Categorized dioxin-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted mean, difference of adjusted means, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table N-2-32 for further analysis of this interaction.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤10 ppt.
Background (Ranch Hand): Current Dioxin ≤10 ppt.
Low (Ranch Hand): Current Dioxin >10 ppt, 10 ppt < Initial Dioxin ≤143 ppt.
High (Ranch Hand): Current Dioxin >10 ppt, Initial Dioxin >143 ppt.

Table 18-57. (Continued)
Analysis of Serum C Peptide (ng/ml) (Diabetics)
(Continuous)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED						
	Current Dioxin Category Mean[b]/(n)			Analysis Results for Log_2 (Current Dioxin + 1)		
Model[a]	Low	Medium	High	R^2	Slope (Std. Error)	p-Value
4	8.24 (26)	9.92 (52)	9.45 (52)	0.617	0.140 (0.240)	0.561
5	8.11 (24)	10.11 (50)	9.31 (56)	0.617	0.138 (0.200)	0.489
6[c]	7.98 (24)	10.07 (50)	9.40 (56)	0.618	0.188 (0.226)	0.408

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED							
	Current Dioxin Category Adjusted Mean/(n)			Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	Low	Medium	High	R^2	Adj. Slope (Std. Error)	p-Value	Covariate Remarks
4	7.39 (24)	8.22 (51)	7.63 (50)	0.689	-0.234 (0.255)	0.360	RACE (p=0.071) BFAT (p=0.002) FAMDIAB (p=0.124) DIABSEV (p=0.006) FAST (p<0.001)
5	7.59 (22)	8.28 (49)	7.47 (54)	0.690	-0.212 (0.212)	0.319	RACE (p=0.069) BFAT (p=0.001) FAMDIAB (p=0.126) DIABSEV (p=0.006) FAST (p<0.001)
6[d]	7.20 (22)	8.13 (49)	7.65 (54)	0.691	-0.125 (0.241)	0.605	RACE (p=0.063) BFAT (p=0.001) FAMDIAB (p=0.127) DIABSEV (p=0.006) FAST (p<0.001)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Adjusted for fasting status.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤46 ppq; Medium = >46-128 ppq; High = >128 ppq.

18-57(b): p=0.077, Diff. of Adj. Means=0.85 and p=0.092, Diff. of Adj. Means=1.20 respectively). Adjusted contrasts within the officer and enlisted flyer strata remained nonsignificant (p>0.48 for each contrast).

Unadjusted analysis of continuous serum C peptide was not significant for Model 2 (Table 18-57(c): p=0.133, Est. Slope=-0.469). Results were marginally significant after adjustment for race, diabetic severity, and fasting status (Table 18-57(d): p=0.069, Adj. Slope=-0.569).

A significant difference in adjusted means from the low Ranch Hand and Comparison categories was revealed in the Model 3 unadjusted analysis (Table 18-57(e): p=0.017, Diff. of Adj. Mean=1.78). The low Ranch Hand and Comparison adjusted means were 10.40 and 8.62 ng/ml respectively. A difference of adjusted means was marginally significant for the low plus high Ranch Hand versus Comparison unadjusted contrast (Table 18-57(e): p=0.073, Diff. of Adj. Mean=1.06). The adjusted mean for the low plus high stratum was 9.68 ng/ml. Similar results were reflected in the adjusted analysis, except that the low plus high Ranch Hand contrast became significant (Table 18-57(f): p=0.008, Diff. of Adj. Mean=1.94 and p=0.038, Diff. of Adj. Means =1.19 respectively for the low Ranch Hand contrast and the low plus high Ranch Hand contrast). The remaining Model 3 contrasts were nonsignificant for both the unadjusted and adjusted analyses (Table 18-57(e,f): p>0.57 for all remaining contrasts). There was a significant interaction between categorized dioxin and occupation (p=0.023). Table N-2-32 presents results stratified by occupation. Adjusted results are based on the final model after deletion of the interaction. Race, body fat, family history of diabetes, diabetic severity, and fasting status were also significant covariates in Model 3.

All tests of association between current dioxin and continuous serum C peptide were nonsignificant for the Models 4, 5, and 6, unadjusted and adjusted analyses (Table 18-57(g,h): p>0.31 for each analysis). Each final adjusted model adjusted for race, body fat, family history of diabetes, diabetic severity, and fasting status.

Serum C Peptide (Discrete)

Model 1 analysis of discrete serum C peptide exhibited no significant difference between Ranch Hands and Comparisons for all unadjusted and adjusted contrasts (Table 18-58(a,b): p>0.25 for each contrast). Age, diabetic severity, and the personality type-by-family history of diabetes and the family history of diabetes-by-body fat interactions were significant covariates in the final adjusted model.

Model 2 analyses of discrete serum C peptide also were nonsignificant for both the unadjusted and adjusted models (Table 18-58(c,d): p>0.13 for both analyses). The adjusted analysis retained race, body fat, and the personality type-by-family history of diabetes and the personality type-by-diabetic severity interactions in the final adjusted model. After exclusion of body fat from the adjusted model, results became marginally significant (Table N-3-42(a): p=0.099, Adj. RR=0.73).

Each difference examined between Ranch Hands and Comparisons was found to be nonsignificant in the Model 3 unadjusted analysis of discrete serum C peptide (Table

Table 18-58.
Analysis of Serum C Peptide (Diabetics)
(Discrete)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Abnormal High**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***134***	***61.2***	***1.00 (0.63,1.59)***	***0.999***
	Comparison	***173***	***61.3***		
Officer	Ranch Hand	52	63.5	0.94 (0.43,2.06)	0.999
	Comparison	57	64.9		
Enlisted Flyer	Ranch Hand	23	56.5	1.09 (0.38,3.16)	0.999
	Comparison	35	54.3		
Enlisted Groundcrew	Ranch Hand	59	61.0	0.97 (0.49,1.93)	0.999
	Comparison	81	61.7		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***1.39 (0.78,2.48)***	***0.259***	AGE (p=0.043)
Officer	1.17 (0.44,3.11)	0.752	DIABSEV (p<0.001)
Enlisted Flyer	1.48 (0.39,5.63)	0.565	PERS*FAMDIAB (p=0.028)
Enlisted Groundcrew	1.50 (0.64,3.53)	0.348	FAMDIAB*BFAT (p=0.001)

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 18-58. (Continued)
Analysis of Serum C Peptide (Diabetics)
(Discrete)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Abnormal High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	29	69.0	0.79 (0.56,1.09)	0.140
Medium	29	69.0		
High	33	48.5		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
89	0.74 (0.48,1.12)	0.138	RACE (p=0.103) BFAT (p=0.006) PERS*FAMDIAB (p<0.001) PERS*DIABSEV (p=0.040)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 18-58. (Continued)
Analysis of Serum C Peptide (Diabetics)
(Discrete)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Percent Abnormal High	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	143	63.6		
Background RH	39	56.4	0.82 (0.38,1.74)	0.597
Low RH	46	69.6	1.47 (0.70,3.08)	0.308
High RH	45	53.3	0.65 (0.32,1.31)	0.228
Low plus High RH	91	61.5	0.97 (0.55,1.70)	0.914

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	143			DXCAT*AGE ($p<0.001$) AGE*DIABSEV ($p<0.001$) OCC*BFAT ($p<0.001$) PERS*BFAT ($p=0.025$)
Background RH	39	****	****	
Low RH	46	****	****	
High RH	45	****	****	
Low plus High RH	91	****	****	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

**** Categorized dioxin-by-covariate interaction ($p \leq 0.01$); adjusted relative risk, confidence interval, and p-value not presented; refer to Appendix Table N-2-33 for further analysis of this interaction.

Note: RH = Ranch Hand.
Comparison: Current Dioxin $\leq$ 10 ppt.
Background (Ranch Hand): Current Dioxin $\leq$ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin $\leq$ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 18-58. (Continued)
Analysis of Serum C Peptide (Diabetics)
(Discrete)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Abnormal High/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	57.7 (26)	65.4 (52)	55.8 (52)	0.96 (0.77,1.21)	0.731
5	54.2 (24)	66.0 (50)	57.1 (56)	0.98 (0.81,1.19)	0.860
6[c]	54.2 (24)	66.0 (50)	57.1 (56)	1.01 (0.82,1.26)	0.909

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	125	0.75 (0.53,1.08)	0.111	RACE (p=0.050) BFAT (p<0.001) DIABSEV (p<0.001) OCC*PERS (p=0.030) PERS*FAMDIAB (p=0.008)
5	125	0.79 (0.59,1.06)**	0.118**	CURR*AGE (p=0.026) CURR*DIABSEV (p=0.007) RACE (p=0.084) BFAT (p<0.001) OCC*PERS (p=0.034) PERS*FAMDIAB (p=0.006)
6[d]	125	0.84 (0.60,1.17)**	0.296**	CURR*AGE (p=0.029) CURR*DIABSEV (p=0.008) RACE (p=0.084) BFAT (p<0.001) OCC*PERS (p=0.035) PERS*FAMDIAB (p=0.006)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.
[b] Relative risk for a twofold increase in current dioxin.
[c] Adjusted for log_2 total lipids.
[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interaction ($0.01<p\leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table N-2-33 for further analysis of this interaction.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

18-58(e): p>0.22 for each contrast). Adjusted Model 3 results revealed a significant interaction between categorized dioxin and age. Results stratified by each age category are presented in Table N-2-33. Other significant covariates in the final adjusted model were the age-by-diabetic severity, the occupation-by-body fat, and the personality type-by-body fat interactions. After body fat was deleted from the final model, the contrast involving younger background Ranch Hands and Comparisons became significant (Appendix Table N-4-14: p=0.042, Adj. RR=0.08) whereas the contrast involving older low Ranch Hands and Comparisons became nonsignificant (p=0.205).

All results from the analysis of discrete serum C peptide from Models 4, 5, and 6 were nonsignificant (Table 18-58(g,h): p>0.11 for both unadjusted and adjusted analyses). Each adjusted model retained race, body fat, and the occupation-by-personality type and personality type-by-family history of diabetes interactions in the final model. Model 4 additionally adjusted for diabetic severity and Models 5 and 6 each additionally adjusted for the current dioxin-by-age (p=0.026 for Model 5 and p=0.029 for Model 6) and current dioxin-by-diabetic severity interactions (p=0.007 for Model 5 and p=0.008 for Model 6). Adjusted results for Models 5 and 6 are based on the final model after deletion of the aforementioned interactions. Results stratified by age and by diabetic severity are presented in Table N-2-33. For Model 5, excluding occupation and body fat from the final analysis caused the association with current dioxin to become nonsignificant in the diabetic severity category of no treatment or diet only (Appendix Table N-4-14: p=0.154). Additionally, for Model 6, the relative risk for the no treatment or diet only category became nonsignificant (Appendix Table N-4-14: p=0.269), and the relative risk for the oral hypoglycemic or insulin dependent category became marginally significant (p=0.098, Adj. RR=1.42) after occupation and body fat were removed.

Total Testosterone (Continuous)

An overall difference between Ranch Hands and Comparisons was not evident in the Model 1 unadjusted analysis of total testosterone measured continuously (Table 18-59: p=0.108). However, when investigated within the levels of occupation, Ranch Hands in the enlisted flyer category had a marginally greater mean level of total testosterone than Comparisons (p=0.055, Diff. of Means=38.03). Mean total testosterone for Ranch Hands in the enlisted flyer category was 526.7 ng/dl in contrast to 488.71 ng/dl for Comparisons. Other contrasts were nonsignificant (p>0.27 for the remaining contrasts). Adjusting for covariate information revealed a significant group-by-age interaction (Table 18-59(b): p=0.039). When this interaction was removed from the final model, a significant difference in mean total testosterone was again revealed for Ranch Hands (528.0 ng/dl) versus Comparisons (490.3 ng/dl) in the enlisted flyer category (p=0.038, Diff. of Adj. Means=37.7). Appendix Table N-2-34 presents stratified results of the group-by-age interaction. In the adjusted analysis, other significant covariates included body fat and occupation.

The unadjusted analysis for Model 2 did not show a significant relationship between initial dioxin and total testosterone in its continuous form (Table 18-59(c): p=0.825). Adjusting for covariates revealed a significant interaction between initial dioxin and personality type (Table 18-59(d): p=0.036). After removal of the interaction from the final model, the adjusted results for Model 2 were nonsignificant (p=0.200). Stratified results of

Table 18-59.
Analysis of Total Testosterone (ng/dl)
(Continuous)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***936***	***510.7***	***12.7 --***	***0.108***
	Comparison	***1,271***	***498.0***		
Officer	Ranch Hand	357	497.4	12.9 --	0.277
	Comparison	500	484.5		
Enlisted Flyer	Ranch Hand	161	526.7	38.0 --	0.055
	Comparison	200	488.7		
Enlisted Groundcrew	Ranch Hand	418	516.1	2.7 --	0.829
	Comparison	571	513.4		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Group	n	Adj. Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]	Covariate Remarks[d]
All	***Ranch Hand***	***936***	***510.0***	***11.1 --*****	***0.131*****	GROUP*AGE (p=0.039)
	Comparison	***1,271***	***498.9***			BFAT (p<0.001)
Officer	Ranch Hand	357	502.3	16.5 --**	0.159**	OCC (p=0.081)
	Comparison	500	485.9			
Enlisted Flyer	Ranch Hand	161	528.0	37.7 --**	0.038**	
	Comparison	200	490.3			
Enlisted Groundcrew	Ranch Hand	418	509.5	-3.5 --**	0.753**	
	Comparison	571	513.0			

[a] Transformed from the square root scale.

[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.

[c] P-values based on difference of means on square root scale.

[d] Covariates and associated p-values correspond to final model based on all participants with available data.

** Group-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted mean, difference of adjusted means, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table N-2-34 for further analysis of this interaction.

Table 18-59. (Continued)
Analysis of Total Testosterone (ng/dl)
(Continuous)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	172	505.9	498.2	0.114	0.0286 (0.1289)	0.825
Medium	170	484.9	482.7			
High	173	477.9	487.6			

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED						
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[d]			
Initial Dioxin	n	Adj. Mean[ad]	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
Low	171	536.0**	0.184	-0.1868 (0.1456)**	0.200**	INIT*PERS (p=0.036) AGE (p=0.060) RACE (p=0.057) BFAT (p<0.001) OCC*PERS (p=0.006)
Medium	170	500.1**				
High	173	486.1**				

[a] Transformed from square root scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Slope and standard error based on square root of total testosterone versus log_2 (initial dioxin).

[d] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Log_2 (initial dioxin)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted mean, adjusted slope, standard error, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table N-2-34 for further analysis of this interaction.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 18-59. (Continued)
Analysis of Total Testosterone (ng/dl)
(Continuous)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED					
Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,056	497.8	498.3		
Background RH	364	540.2	521.4	23.0 --	0.031
Low RH	256	503.4	510.5	12.2 --	0.314
High RH	259	475.9	492.3	-6.0 --	0.614
Low plus High RH	515	489.5	501.3	3.0 --	0.749

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED					
Dioxin Category	n	Adj. Mean[ae]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]	Covariate Remarks
Comparison	1,056	514.4			AGE ($p<0.001$) RACE ($p=0.054$) OCC ($p=0.039$) BFAT ($p<0.001$)
Background RH	364	545.9	31.5 --	0.004	
Low RH	256	529.5	15.1 --	0.214	
High RH	259	491.4	-23.0 --	0.061	
Low plus High RH	515	510.2	-4.2 --	0.651	

[a] Transformed from square root scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Difference of adjusted means after transformation to original scale; confidence interval on difference of adjusted means not presented because analysis was performed on square root scale.

[d] P-value is based on difference of means on square root scale.

[e] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 18-59. (Continued)
Analysis of Total Testosterone (ng/dl)
(Continuous)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED						
	Current Dioxin Category Mean[a]/(n)			Analysis Results for Log_2 (Current Dioxin + 1)		
Model[b]	Low	Medium	High	R^2	Slope (Std. Error)[c]	p-Value
4	545.3 (287)	508.4 (295)	479.1 (297)	0.023	-0.4277 (0.0951)	<0.001
5	550.2 (292)	504.2 (293)	477.7 (294)	0.035	-0.4561 (0.0811)	<0.001
6[d]	539.0 (291)	503.3 (293)	487.5 (294)	0.042	-0.3385 (0.0870)	<0.001

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED							
	Current Dioxin Category Adjusted Mean[a]/(n)			Analysis Results for Log_2 (Current Dioxin + 1)			
Model[b]	Low	Medium	High	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
4	**** (287)	**** (295)	**** (297)	0.161	****	****	CURR*OCC (p=0.007) BFAT (p<0.001) AGE*RACE (p=0.035)
5	548.9** (292)	523.4** (293)	493.4** (294)	0.166	-0.3396 (0.0912)**	<0.001**	CURR*OCC (p=0.014) BFAT (p<0.001) AGE*RACE (p=0.034)
6[e]	535.81** (291)	519.10** (293)	488.80** (294)	0.168	-0.2262 (0.0976)**	0.021**	CURR*OCC (p=0.030) BFAT (p<0.001) AGE*RACE (p=0.031)

[a] Transformed from square root scale.

[b] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[c] Slope and standard error based on square root of total testosterone versus log_2 (current dioxin + 1).

[d] Adjusted for log_2 total lipids.

[e] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interaction ($0.01<p\leq0.05$); adjusted mean, adjusted slope, standard error, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table N-2-34 for further analysis of this interaction.

**** Log_2 (current dioxin + 1)-by-covariate interaction ($p\leq0.01$); adjusted mean, adjusted slope, standard error and p-value not presented; refer to Appendix Table N-2-34 for further analysis of this interaction.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

the interaction are presented in Appendix Table N-2-34. Age, race, body fat, and the occupation-by-personality type interaction also were significant in the final adjusted model.

The unadjusted analysis for Model 3 revealed a significant difference in total testosterone means between the background Ranch Hands (521.4 ng/dl) and the Comparisons (498.3 ng/dl) (Table 18-59(e): p=0.031). The adjusted analysis for Model 3 also revealed a significant difference in total testosterone means between the background Ranch Hands (545.9 ng/dl) and the Comparisons (514.4 ng/dl), as well as a difference in means between Ranch Hands in the high dioxin category (491.4 ng/dl) and Comparisons (Table 18-59(f): p=0.004 and p=0.061 respectively). The covariates age, race, occupation, and body fat were accounted for in the final adjusted model. After the exclusion of occupation and body fat from the final model, the contrast between high Ranch Hands and Comparisons was no longer significant (Appendix Table N-3-43: p=0.290).

The unadjusted analyses for Models 4 through 6 showed highly significant negative relationships between current dioxin and total testosterone in its continuous form (Table 18-59(g): Model 4: p<0.001, Slope=-0.4277; Model 5: p<0.001, Slope=-0.4561; and Model 6: p<0.001, Slope=-0.3385). In Model 4, the unadjusted means in the low, medium, and high current dioxin categories were 545.3, 508.4, and 479.1 ng/dl, for Model 5 the unadjusted means were 550.2, 504.2, and 477.7 ng/dl, and in Model 6, the unadjusted means were 539.0, 503.3, and 487.5 ng/dl. The adjusted analyses of Models 4, 5, and 6 each revealed significant current dioxin-by-occupation interactions (Table 18-59(h): p=0.007, p=0.014, and p=0.030 respectively). Body fat and the age-by-race interaction also were significant in the final adjusted model for each of Models 4 through 6. Removing the current dioxin-by-occupation interaction in Models 5 and 6 revealed significant negative relationships between current dioxin and total testosterone (Table 18-59(h): Model 5: p<0.001, Slope=-0.3396 and Model 6: p=0.021, Slope=-0.2262). Stratified analyses were performed by occupation to further investigate the current dioxin-by-occupation interactions. These results are presented in Appendix Table N-2-34. In Model 4, the officers and enlisted flyers both showed significant decreases in total testosterone for increasing levels of current dioxin (Appendix Table N-2-34: Officers p<0.001, Slope=-0.9913 and Enlisted Flyers p=0.035, Slope=-0.6173).

Total Testosterone (Discrete)

Results from the Model 1 unadjusted discrete analysis of total testosterone were nonsignificant (Table 18-60: p>0.48 for all contrasts). Two significant group interactions involving race and personality type were revealed after adjustment was made for covariates (Table 18-60(b): p=0.040 and p=0.002 respectively). Deleting these interactions from the final model did not lead to significant differences between Ranch Hands and Comparisons (p>0.20 for all contrasts). The group-by-race and group-by-personality type interactions were analyzed for significant differences between Ranch Hands and Comparisons within each stratum, and results are shown in Appendix Table N-2-35. Age and body fat also were retained in the adjusted analysis.

The unadjusted analyses for Models 2 and 3 did not reveal any significant relationships between discretized total testosterone and dioxin (Table 18-60(c,e): p>0.28 for the unadjusted analyses). The adjusted analysis for Model 2 revealed a significant initial dioxin-by-

Table 18-60.
Analysis of Total Testosterone
(Discrete)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Abnormal Low**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***936***	***4.6***	***0.85 (0.58,1.26)***	***0.481***
	Comparison	***1,271***	***5.4***		
Officer	Ranch Hand	357	4.8	1.04 (0.55,1.97)	0.999
	Comparison	500	4.6		
Enlisted Flyer	Ranch Hand	161	3.7	0.67 (0.24,1.84)	0.589
	Comparison	200	5.5		
Enlisted Groundcrew	Ranch Hand	418	4.8	0.79 (0.45,1.40)	0.510
	Comparison	571	6.0		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***0.83 (0.55,1.25)****	***0.374****	GROUP*RACE (p=0.040) GROUP*PERS (p=0.002) AGE (p=0.028) BFAT (p<0.001)
Officer	0.99 (0.51,1.93)**	0.973**	
Enlisted Flyer	0.50 (0.17,1.45)**	0.202**	
Enlisted Groundcrew	0.82 (0.45,1.49)**	0.514**	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

** Group-by-covariate interactions ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of these interactions; refer to Appendix Table N-2-35 for further analysis of these interactions.

Table 18-60. (Continued)
Analysis of Total Testosterone
(Discrete)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Abnormal Low	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	172	4.7	1.05 (0.80,1.38)	0.709
Medium	170	4.7		
High	173	8.1		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
515	1.16 (0.84,1.59)**	0.364**	INIT*OCC (p=0.033) RACE (p=0.058) BFAT (p=0.045)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Log_2 (initial dioxin)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table N-2-35 for further analysis of this interaction.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 18-60. (Continued)
Analysis of Total Testosterone
(Discrete)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	**n**	**Percent Abnormal Low**	**Est. Relative Risk (95% C.I.)[ab]**	**p-Value**
Comparison	1,056	5.2		
Background RH	364	2.7	0.69 (0.34,1.38)	0.289
Low RH	256	4.3	0.70 (0.35,1.39)	0.308
High RH	259	7.3	1.14 (0.65,2.01)	0.645
Low plus High RH	515	5.8	0.93 (0.58,1.49)	0.751

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	**n**	**Adj. Relative Risk (95% C.I.)[ac]**	**p-Value**	**Covariate Remarks**
Comparison	1,055			DXCAT*PERS (p=0.015) AGE (p=0.012) RACE (p=0.084) BFAT (p<0.001)
Background RH	364	0.64 (0.32,1.30)**	0.222**	
Low RH	255	0.65 (0.32,1.30)**	0.222**	
High RH	259	1.29 (0.73,2.29)**	0.386**	
Low plus High RH	514	0.95 (0.59,1.54)**	0.830**	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Categorized dioxin-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table N-2-35 for further analysis of this interaction.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 18-60. (Continued)
Analysis of Total Testosterone
(Discrete)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Abnormal Low/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	2.4 (287)	4.1 (295)	7.1 (297)	1.25 (1.02,1.54)	0.033
5	2.4 (292)	4.1 (293)	7.1 (294)	1.27 (1.05,1.53)	0.012
6[c]	2.4 (291)	4.1 (293)	7.1 (294)	1.20 (0.99,1.47)	0.071

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	878	1.13 (0.85,1.49)**	0.398**	CURR*OCC (p=0.033) RACE (p=0.025) PERS (p=0.120) BFAT (p<0.001)
5	878	1.11 (0.90,1.36)	0.322	RACE (p=0.030) PERS (p=0.103) BFAT (p<0.001)
6[d]	877	1.06 (0.85,1.31)	0.632	RACE (p=0.035) PERS (p=0.130) BFAT (p<0.001)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table N-2-35 for further analysis of this interaction.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

occupation interaction (Table 18-60(d): p=0.033). After the interaction was removed from the final adjusted model, the results did not reveal a significant association between total testosterone and initial dioxin (p=0.364). Race and body fat were significant covariates in the final adjusted model. Stratified results of the interaction are presented in Appendix Table N-2-35. Adjusting for covariates in Model 3 revealed a significant categorized dioxin-by-personality type interaction (Table 18-60(f): p=0.015). After removal of the interaction from the final model, the analysis did not show a significant relationship between total testosterone and categorized dioxin (p>0.22 for all adjusted analyses). For further investigation of the interaction, stratified analyses were performed by personality type, and the results are displayed in Appendix Table N-2-35.

The unadjusted analyses of Models 4, 5, and 6 showed significant, or marginally significant, positive associations between current dioxin and discretized total testosterone (Table 18-60(g): p=0.033, Est. RR=1.25; p=0.012, Est. RR=1.27; and p=0.071, Est. RR=1.20 respectively). In Models 4 through 6, the percentage of individuals with abnormally low total testosterone levels in the low, medium, and high categories were 2.4, 4.1, and 7.1 percent. Adjusting for covariates in Model 4 revealed a significant current dioxin-by-occupation interaction (Table 18-60(f): p=0.033). Race, personality type, and body fat also were retained in the final adjusted model. Stratified results of the interaction are presented in Appendix Table N-2-35. After removing the interaction from the model, the results of the analysis were nonsignificant (p=0.398). However, after excluding occupation and body fat from the adjusted Model 4 analysis, the results showed a significant association between current dioxin and total testosterone (Appendix Table N-3-44: p=0.027, Adj. RR=1.26). The adjusted analyses for Models 5 and 6 did not reveal any significant associations between current dioxin and total testosterone (Table 18-60(f): p>0.32 for adjusted analyses). The covariates race, personality type, and body fat were significant in the final adjusted models. Similar to Model 4, excluding body fat from the final models in Models 5 and 6 revealed significant positive associations between current dioxin and total testosterone (Appendix Table N-3-44: p=0.011, Adj. RR=1.27 for Model 5 and p=0.055, Adj. RR=1.22 for Model 6).

Free Testosterone (Continuous)

The Model 1 unadjusted analysis of free testosterone did not reveal significant differences between Ranch Hands and Comparisons (Table 18-61(a): p>0.13). After adjustment was made for age, personality type, body fat, and the race-by-occupation interaction, a marginally significant difference between the two groups was revealed in the enlisted flyer category with Ranch Hands possessing a greater mean level of free testosterone (20.10 pg/ml) than Comparisons (19.09 pg/ml) (Table 18-61(b): p=0.097, Diff. of Adj. Mean=1.01).

In Model 2, the unadjusted and adjusted analyses did not reveal a significant association between initial dioxin and free testosterone in its continuous form (Table 18-61(c,d): p>0.12 for unadjusted and adjusted analyses). Race, occupation, and an age-by-body fat interaction were significant in the final adjusted model.

The unadjusted analysis for Model 3 revealed a significant difference in means adjusted for percent body fat at time of duty in SEA, and change in percent body fat from time of

Table 18-61.
Analysis of Free Testosterone (pg/ml)
(Continuous)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	*Ranch Hand*	*936*	*18.70*	*0.39 --*	*0.138*
	Comparison	*1,271*	*18.31*		
Officer	Ranch Hand	357	17.55	0.31 --	0.429
	Comparison	500	17.24		
Enlisted Flyer	Ranch Hand	161	19.19	0.91 --	0.145
	Comparison	200	18.28		
Enlisted Groundcrew	Ranch Hand	418	19.52	0.23 --	0.576
	Comparison	571	19.29		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Group	n	Adj. Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]	Covariate Remarks[d]
All	*Ranch Hand*	*935*	*19.56*	*0.34 --*	*0.170*	AGE (p<0.001)
	Comparison	*1,270*	*19.22*			PERS (p=0.016)
Officer	Ranch Hand	357	20.17	0.41 --	0.311	BFAT (p<0.001)
	Comparison	500	19.76			RACE*OCC (p=0.026)
Enlisted Flyer	Ranch Hand	160	20.10	1.01 --	0.097	
	Comparison	200	19.09			
Enlisted Groundcrew	Ranch Hand	418	18.67	0.04 --	0.921	
	Comparison	570	18.63			

[a] Transformed from the square root scale.

[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.

[c] P-values based on difference of means on square root scale.

[d] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 18-61. (Continued)
Analysis of Free Testosterone (pg/ml)
(Continuous)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	172	18.41	18.26	0.070	0.030 (0.023)	0.187
Medium	170	18.31	18.21			
High	173	18.81	19.07			

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED						
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[d]			
Initial Dioxin	n	Adj. Mean[ad]	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
Low	172	20.20	0.201	-0.038 (0.025)	0.121	RACE (p=0.017) OCC (p=0.076) AGE*BFAT (p=0.018)
Medium	170	19.18				
High	173	18.94				

[a] Transformed from square root scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Slope and standard error based on square root of free testosterone versus log_2 (initial dioxin).

[d] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 18-61. (Continued)
Analysis of Free Testosterone (pg/ml)
(Continuous)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED					
Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,056	18.31	18.32		
Background RH	364	18.82	18.30	-0.02 --	0.954
Low RH	256	18.25	18.52	0.20 --	0.640
High RH	259	18.78	19.21	0.89 --	0.033
Low plus High RH	515	18.51	18.86	0.54 --	0.093

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED					
Dioxin Category	n	Adj. Mean[ae]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]	Covariate Remarks
Comparison	1,055	19.27			AGE (p<0.001) PERS (p=0.050) BFAT (p<0.001) OCC*RACE (p=0.039)
Background RH	364	19.75	0.48 --	0.184	
Low RH	255	19.66	0.39 --	0.336	
High RH	259	19.18	-0.09 --	0.826	
Low plus High RH	514	19.42	0.15 --	0.640	

[a] Transformed from square root scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Difference of adjusted means after transformation to original scale; confidence interval on difference of adjusted means not presented because analysis was performed on square root scale.

[d] P-value is based on difference of means on square root scale.

[e] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 18-61. (Continued)
Analysis of Free Testosterone (pg/ml)
(Continuous)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[b]	Current Dioxin Category Mean[a]/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) R^2	Slope (Std. Error)[c]	p-Value
4	18.69 (287)	18.53 (295)	18.72 (297)	0.001	-0.014 (0.016)	0.383
5	18.97 (292)	18.19 (293)	18.77 (294)	<0.001	-0.008 (0.014)	0.546
6[d]	18.88 (291)	18.19 (293)	18.84 (294)	0.001	-0.003 (0.015)	0.818

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[b]	Current Dioxin Category Adjusted Mean[a]/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
4	19.48 (287)	19.92 (294)	19.22 (297)	0.162	-0.009 (0.018)	0.627	AGE (p<0.001) OCC (p=0.040) RACE (p=0.046) PERS (p=0.108) BFAT (p<0.001)
5	19.77 (292)	19.54 (292)	19.45 (294)	0.162	-0.006 (0.015)	0.683	AGE (p<0.001) OCC (p=0.042) RACE (p=0.046) PERS (p=0.107) BFAT (p<0.001)
6[e]	19.83 (291)	19.56 (292)	19.40 (294)	0.093	-0.009 (0.016)	0.599	AGE (p<0.001) OCC (p=0.044) RACE (p=0.043) PERS (p=0.116) BFAT (p<0.001)

[a] Transformed from square root scale.

[b] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[c] Slope and standard error based on square root of free testosterone versus log_2 (current dioxin + 1).

[d] Adjusted for log_2 total lipids.

[e] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

duty in SEA to date of the blood draw for dioxin, between Ranch Hands in the high dioxin category (19.21 pg/ml) and Comparisons (18.32 pg/ml), as well as a marginally significant difference in means between Ranch Hands in the low plus high category (18.86 pg/ml) and Comparisons (Table 18-61(e): p=0.033 and p=0.093 respectively). The adjusted analysis did not exhibit a significant relationship between categorized dioxin and free testosterone (Table 18-61(f): p>0.18 for all adjusted contrasts). The final adjusted model contained the covariates age, personality type, body fat, and an occupation-by-race interaction.

In Models 4 through 6, the unadjusted and adjusted analyses did not reveal any significant associations between current dioxin and free testosterone in its continuous form (Table 18-61(g,h): p>0.38 for all analyses). However, after occupation and body fat were excluded from the final adjusted model, Models 4 through 6 revealed significant negative associations between current dioxin and free testosterone (Appendix Table N-3-45: p=0.037, slope=-0.033 for Model 4; p=0.033, Slope=-0.029 for Model 5; and p=0.044, Slope=-0.030 for Model 6). Significant covariates for the adjusted analyses in Models 4 through 6 were age, occupation, race, personality type, and body fat.

Free Testosterone (Discrete)

Comparisons had a greater overall percentage of abnormalities than Ranch Hands in the unadjusted discrete analysis of free testosterone (Table 18-62(a): p=0.014, Est. RR=0.75). After stratifying the analysis across occupation, the difference between the two groups was significant in the enlisted flyer category (p=0.012, Est. RR=0.42). Adjustment for age, personality type, and body fat led to similar results in the adjusted analysis. A significantly greater percentage of Comparisons possessed abnormally low free testosterone than Ranch Hands, both overall and for enlisted flyers (Table 18-62(b): p=0.017, Adj. RR=0.76 for overall contrast and p=0.006, Adj. RR=0.39 for enlisted flyer contrast).

The unadjusted and adjusted analyses for Model 2 did not reveal a significant relationship between initial dioxin and free testosterone (Table 18-62(c,d): p>0.12). The covariate body fat was significant in the final adjusted model as well as the interactions age-by-race, race-by-occupation, and race-by-personality type.

The unadjusted analysis for Model 3 revealed marginally significant differences between Ranch Hands in the background category and Comparisons and between Ranch Hands in the low category and Comparisons (Table 18-62(e): p=0.084, Est. RR=0.74 and p=0.061, Est. RR=0.69 respectively). The percentage of participants with abnormally low free testosterone levels in the Comparison, background Ranch Hand, and low Ranch Hand categories were 19.3, 13.5, and 14.8 percent respectively. The background Ranch Hand and low Ranch Hand contrasts remained marginally significant in the adjusted analysis (Table 18-62(f): p=0.089, Adj. RR=0.74 and p=0.093, Adj. RR=0.72). Age, occupation, personality type, and body fat were significant in the final adjusted model. After occupation and body fat were excluded from the final model, the background Ranch Hands versus Comparisons contrast was no longer significant (Appendix Table N-3-46: p=0.136); however, the low plus high Ranch Hands versus Comparisons contrast became marginally significant (p=0.095, Adj. RR=0.79).

Table 18-62.
Analysis of Free Testosterone
(Discrete)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Percent Abnormal Low	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***936***	***15.4***	***0.75 (0.60,0.94)***	***0.014***
	Comparison	***1,271***	***19.5***		
Officer	Ranch Hand	357	15.1	0.76 (0.53,1.10)	0.166
	Comparison	500	19.0		
Enlisted Flyer	Ranch Hand	161	8.7	0.42 (0.22,0.81)	0.012
	Comparison	200	18.5		
Enlisted Groundcrew	Ranch Hand	418	18.2	0.87 (0.63,1.20)	0.449
	Comparison	571	20.3		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks[a]
All	***0.76 (0.60,0.95)***	***0.017***	AGE (p=0.002) PERS (p=0.018) BFAT (p<0.001)
Officer	0.76 (0.52,1.10)	0.145	
Enlisted Flyer	0.39 (0.20,0.76)	0.006	
Enlisted Groundcrew	0.91 (0.65,1.26)	0.570	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

**Table 18-62. (Continued)
Analysis of Free Testosterone
(Discrete)**

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Abnormal Low	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	172	13.4	1.14 (0.96,1.36)	0.129
Medium	170	17.1		
High	173	21.4		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
514	1.15 (0.94,1.41)	0.180	BFAT (p=0.034) AGE*RACE (p=0.001) RACE*OCC (p=0.025) RACE*PERS (p<0.001)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 18-62. (Continued)
Analysis of Free Testosterone
(Discrete)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Abnormal Low	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,056	19.3		
Background RH	364	13.5	0.74 (0.52,1.04)	0.084
Low RH	256	14.8	0.69 (0.47,1.02)	0.061
High RH	259	19.7	0.91 (0.64,1.29)	0.582
Low plus High RH	515	17.3	0.80 (0.60,1.06)	0.121

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,055			AGE (p=0.015) OCC (p=0.148) PERS (p=0.078) BFAT (p=0.025)
Background RH	364	0.74 (0.52,1.05)	0.089	
Low RH	255	0.72 (0.49,1.06)	0.093	
High RH	259	0.90 (0.63,1.30)	0.588	
Low plus High RH	514	0.81 (0.61,1.08)	0.147	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 18-62. (Continued)
Analysis of Free Testosterone
(Discrete)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Abnormal/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	13.2 (287)	14.2 (295)	19.5 (297)	1.20 (1.06,1.35)	0.004
5	12.7 (292)	15.7 (293)	18.7 (294)	1.15 (1.04,1.29)	0.009
6[c]	12.7 (291)	15.7 (293)	18.7 (294)	1.21 (1.07,1.36)	0.002

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	879	1.10 (0.94,1.29)	0.227	OCC (p=0.029) BFAT (p<0.001)
5	878	1.05 (0.92,1.21)	0.468	AGE (p=0.140) OCC (p=0.038) PERS (p=0.149) BFAT (p<0.001)
6[d]	878	1.12 (0.97,1.30)	0.131	OCC (p=0.027) BFAT (p<0.001)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

In the unadjusted analyses of Models 4, 5, and 6, highly significant positive associations were found between current dioxin and discretized free testosterone (Table 18-62(g): p=0.004, Est. RR=1.20 for Model 4; p=0.009, Est. RR=1.15 for Model 5; and p=0.002, and Est. RR=1.15 for Model 6). In Model 4, the percentage of Ranch Hands with abnormally low free testosterone levels in the low, medium, and high current dioxin categories were 13.2, 14.2, and 19.5 percent respectively. In both Model 5 and Model 6, the percentage of individuals with abnormally low free testosterone levels in the low, medium, and high categories were 12.7, 15.7, and 18.7 percent respectively. The adjusted analyses for Models 4 through 6 did not reveal any significant relationships between current dioxin and free testosterone. In Models 4 and 6, occupation and body fat were retained in the final adjusted model. In Model 5, age, occupation, personality type, and body fat were retained in the final adjusted model. After occupation and body fat were excluded from the final adjusted models for Models 4 through 6, the results became significant (Appendix Table N-3-46: p=0.004, Adj. RR=1.20 for Model 4; p=0.026, Adj. RR=1.13 for Model 5; and p=0.002, Adj. RR=1.21 for Model 6).

Sex Hormone Binding Globulin

Similar results were revealed in both the unadjusted and adjusted Model 1 analyses of sex hormone binding globulin. In each analysis, the overall and enlisted groundcrew contrasts for Ranch Hands versus Comparisons were at least marginally significant, and the adjusted overall contrast was significant. In each case, Ranch Hands had fewer instances of abnormally low sex hormone binding globulin than Comparisons (Table 18-63(a,b): p=0.051, Est. RR=0.79 for the overall contrast and p=0.077, Est. RR=0.72 for the enlisted groundcrew contrast in the unadjusted analysis; p=0.048, Adj. RR=0.80 for the overall contrast and p=0.080, Adj. RR=0.74 for the enlisted groundcrew contrast in the adjusted analysis). Race, occupation, personality type, and body fat were retained in the adjusted analysis.

In Model 2, the unadjusted and adjusted analyses did not show any significant associations between initial dioxin and sex hormone binding globulin (Table 18-63(c,d): p>0.87 for unadjusted and adjusted analyses). The race-by-occupation interaction was significant in the final adjusted model.

The unadjusted analysis for Model 3 revealed a marginally significant difference between Ranch Hands in the low plus high dioxin category, and Comparisons (Table 18-63(e): p=0.054, Est. RR=0.75). The percentage of individuals with abnormally low levels of sex hormone binding globulins in the low plus high Ranch Hands category and the Comparison group were 15.1 percent and 18.6 percent. Similarly, after adjustment was made for covariates, Model 3 showed a significant difference between Ranch Hands in the low plus high dioxin category and Comparisons (Table 18-63(f): p=0.038, Adj. RR=0.73). Race and personality type were significant in the final adjusted model.

The unadjusted and adjusted analyses for Models 4, 5, and 6 did not show any significant associations between sex hormone binding globulin and current dioxin (Table 18-63(g,h): p>0.65 for unadjusted and adjusted analyses). Body fat was retained in the final adjustment for Model 4. No covariates were significant in Models 5 and 6.

Table 18-63.
Analysis of Sex Hormone Binding Globulin

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Abnormal Low**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***936***	***15.6***	***0.79 (0.63,0.99)***	***0.051***
	Comparison	***1,271***	***18.9***		
Officer	Ranch Hand	357	17.6	0.88 (0.62,1.25)	0.527
	Comparison	500	19.6		
Enlisted Flyer	Ranch Hand	161	13.7	0.80 (0.45,1.44)	0.550
	Comparison	200	16.5		
Enlisted Groundcrew	Ranch Hand	418	14.6	0.72 (0.51,1.02)	0.077
	Comparison	571	19.1		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***0.80 (0.63,1.00)***	***0.048***	OCC (p=0.112) RACE (p=0.007) PERS (p=0.043) BFAT (p=0.030)
Officer	0.88 (0.62,1.25)	0.479	
Enlisted Flyer	0.76 (0.42,1.37)	0.355	
Enlisted Groundcrew	0.74 (0.52,1.04)	0.080	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 18-63. (Continued)
Analysis of Sex Hormone Binding Globulin

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Abnormal Low	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	172	17.4	0.99 (0.82,1.18)	0.871
Medium	170	12.4		
High	173	15.6		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
515	0.99 (0.80,1.22)	0.887	RACE*OCC (p=0.028)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 18-63. (Continued)
Analysis of Sex Hormone Binding Globulin

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Abnormal Low	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,056	18.6		
Background RH	364	17.9	1.02 (0.74,1.39)	0.922
Low RH	256	15.2	0.77 (0.53,1.12)	0.174
High RH	259	15.1	0.74 (0.51,1.07)	0.112
Low plus High RH	515	15.1	0.75 (0.56,1.01)	0.054

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,055			RACE (p=0.051) PERS (p=0.070)
Background RH	364	1.03 (0.75,1.41)	0.845	
Low RH	255	0.74 (0.51,1.08)	0.119	
High RH	259	0.73 (0.50,1.06)	0.101	
Low plus High RH	514	0.73 (0.55,0.98)	0.038	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 18-63. (Continued)
Analysis of Sex Hormone Binding Globulin

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Abnormal Low/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	17.8 (287)	16.3 (295)	14.8 (297)	1.00 (0.88,1.13)	0.994
5	15.1 (292)	18.4 (293)	15.3 (294)	1.02 (0.92,1.14)	0.666
6[c]	15.1 (291)	18.4 (293)	15.3 (294)	0.98 (0.87,1.10)	0.709

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	879	0.97 (0.85,1.11)	0.655	BFAT (p=0.131)
5	879	1.02 (0.92,1.14)	0.666	
6[c]	878	0.98 (0.87,1.10)	0.709	

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Total Testosterone to Sex Hormone Binding Globulin Ratio

Neither the unadjusted nor the adjusted Model 1 analyses of the ratio of total testosterone to sex hormone binding globulin revealed any significant group differences (Table 18-64(a,b): $p>0.21$ for all contrasts). The age-by-body fat interaction was significant in the adjusted analysis.

The unadjusted and adjusted analyses for Models 2 and 3 did not reveal any significant associations between dioxin and the ratio of total testosterone to sex hormone binding globulin (Table 18-64(c-f): $p>0.26$ for unadjusted and adjusted analyses). Age was significant in the final adjusted model for Models 2 and 3.

The unadjusted and adjusted analyses of Models 4 and 5 as well as the unadjusted analysis for Model 6 did not find a significant relationship between current dioxin and the ratio of total testosterone to sex hormone binding globulin (Table 18-64(g,h): $p>0.13$). Age was significant in the final adjusted models for Models 4, 5 and 6. Adjusting for covariates in Model 6 revealed a marginally significant positive relationship between current dioxin and the ratio of total testosterone to sex hormone binding globulin (Table 18-64(h): $p=0.067$, Adj. RR=1.16).

Estradiol (Continuous)

Neither the Model 1 unadjusted nor the adjusted analysis of estradiol detected a significant difference between Ranch Hands and Comparisons (Table 18-65(a): $p>0.40$ for all analyses). Age, race, and occupation were significant in the adjusted analysis.

The unadjusted analysis for Model 2 did not find a significant relationship between initial dioxin and estradiol in its continuous form (Table 18-65(c): $p=0.101$). Adjusting for covariates, however, revealed a marginally significant positive association between initial dioxin and estradiol in Model 2 (Table 18-65(d): $p=0.057$, Slope=0.074). Race was significant in the final adjusted model.

The unadjusted and adjusted analysis of Model 3 did not reveal any significant associations between categorized dioxin and estradiol (Table 18-65(e,f): $p>0.44$ for unadjusted and adjusted analyses). Age and race were significant in the final adjusted model.

The unadjusted and adjusted analyses of Models 4 through 6 did not reveal any significant associations between estradiol and current dioxin (Table 18-65(g,h): $p>0.19$ for unadjusted and adjusted analyses). Age and race were retained in each of the final adjusted models for Models 4, 5, and 6.

Estradiol (Discrete)

The percentage of Ranch Hands with abnormally high estradiol levels was not significantly greater than that of the Comparisons in the Model 1 unadjusted and adjusted analyses (Table 18-66(a,b): $p>0.30$ for all analyses). In the adjusted analysis, race and the occupation-by-age interaction were significant.

Table 18-64.
Analysis of Total Testosterone to Sex Hormone Binding Globulin Ratio

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Abnormal Low**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***936***	***9.1***	***0.85 (0.64,1.14)***	***0.351***
	Comparison	***1,271***	***10.5***		
Officer	Ranch Hand	357	9.2	0.76 (0.49,1.19)	0.280
	Comparison	500	11.8		
Enlisted Flyer	Ranch Hand	161	9.3	0.72 (0.37,1.42)	0.430
	Comparison	200	12.5		
Enlisted Groundcrew	Ranch Hand	418	8.9	1.03 (0.66,1.62)	0.972
	Comparison	571	8.6		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***0.85 (0.63,1.13)***	***0.262***	AGE*BFAT (p=0.034)
Officer	0.75 (0.47,1.18)	0.211	
Enlisted Flyer	0.70 (0.35,1.38)	0.297	
Enlisted Groundcrew	1.05 (0.67,1.66)	0.835	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 18-64. (Continued)
Analysis of Total Testosterone to Sex Hormone Binding Globulin Ratio

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Abnormal Low	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	172	9.3	0.98 (0.79,1.22)	0.879
Medium	170	11.2		
High	173	9.2		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
515	1.08 (0.86,1.36)	0.486	AGE (p=0.004)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 18-64. (Continued)
Analysis of Total Testosterone to Sex Hormone Binding Globulin Ratio

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Abnormal Low	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,056	9.6		
Background RH	364	7.7	0.83 (0.53,1.29)	0.408
Low RH	256	9.8	0.96 (0.61,1.53)	0.876
High RH	259	10.0	1.02 (0.64,1.61)	0.941
Low plus High RH	515	9.9	0.99 (0.69,1.42)	0.957

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,056			AGE (p<0.001)
Background RH	364	0.78 (0.50,1.21)	0.263	
Low RH	256	0.90 (0.57,1.44)	0.671	
High RH	259	1.19 (0.75,1.91)	0.457	
Low plus High RH	515	1.03 (0.72,1.48)	0.865	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 18-64. (Continued)
Analysis of Total Testosterone to Sex Hormone Binding Globulin Ratio

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[a]	Current Dioxin Category Percent Abnormal Low/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) Est. Relative Risk (95% C.I.)[b]	p-Value
4	7.7 (287)	9.2 (295)	10.1 (297)	1.05 (0.90,1.23)	0.514
5	7.2 (292)	11.3 (293)	8.5 (294)	1.03 (0.90,1.18)	0.630
6[c]	7.2 (291)	11.3 (293)	8.5 (294)	1.08 (0.93,1.25)	0.327

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[a]	Analysis Results for Log_2 (Current Dioxin + 1) n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	879	1.14 (0.96,1.34)	0.136	AGE ($p<0.001$)
5	879	1.09 (0.95,1.26)	0.227	AGE ($p<0.001$)
6[d]	878	1.16 (0.99,1.36)	0.067	AGE ($p<0.001$)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 18-65.
Analysis of Estradiol (pg/ml)
(Continuous)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Mean[a]**	**Difference of Means (95% C.I.)[b]**	**p-Value[c]**
All	*Ranch Hand*	*952*	*32.16*	*-0.01 --*	*0.992*
	Comparison	*1,280*	*32.17*		
Officer	Ranch Hand	367	31.24	-0.36 --	0.679
	Comparison	502	31.60		
Enlisted Flyer	Ranch Hand	162	32.68	0.99 --	0.498
	Comparison	202	31.69		
Enlisted Groundcrew	Ranch Hand	423	32.77	-0.06 --	0.943
	Comparison	576	32.83		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED						
Occupational Category	**Group**	**n**	**Adj. Mean[a]**	**Difference of Adj. Means (95% C.I.)[b]**	**p-Value[c]**	**Covariate Remarks[d]**
All	*Ranch Hand*	*952*	*34.22*	*0.01 --*	0.995	AGE ($p<0.001$)
	Comparison	*1,280*	*34.21*			RACE ($p<0.001$)
Officer	Ranch Hand	367	33.52	-0.41 --	0.655	OCC ($p=0.024$)
	Comparison	502	33.93			
Enlisted Flyer	Ranch Hand	162	35.43	1.19 --	0.409	
	Comparison	202	34.24			
Enlisted Groundcrew	Ranch Hand	423	34.11	-0.06 --	0.940	
	Comparison	576	34.18			

[a] Transformed from the square root scale.

[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.

[c] P-values based on difference of means on square root scale.

[d] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 18-65. (Continued)
Analysis of Estradiol (pg/ml)
(Continuous)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	174	32.54	32.64	0.011	0.064 (0.039)	0.101
Medium	173	31.00	31.06			
High	173	33.86	33.70			

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED						
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[d]			
Initial Dioxin	n	Adj. Mean[ad]	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
Low	174	35.77	0.033	0.074 (0.039)	0.057	RACE (p=0.001)
Medium	173	34.41				
High	173	37.22				

[a] Transformed from square root scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Slope and standard error based on square root of estradiol versus log_2 (initial dioxin).

[d] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 18-65. (Continued)
Analysis of Estradiol (pg/ml)
(Continuous)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED					
Dioxin Category	**n**	**Mean[a]**	**Adj. Mean[ab]**	**Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]**	**p-Value[d]**
Comparison	1,063	32.28	32.27		
Background RH	374	31.44	31.66	-0.61 --	0.448
Low RH	260	31.86	31.81	-0.46 --	0.618
High RH	260	33.06	32.84	0.57 --	0.539
Low plus High RH	520	32.46	32.32	0.05 --	0.941

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED					
Dioxin Category	**n**	**Adj. Mean[ae]**	**Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]**	**p-Value[d]**	**Covariate Remarks**
Comparison	1,063	34.80			AGE (p=0.015) RACE (p<0.001)
Background RH	374	34.39	-0.41 --	0.621	
Low RH	260	34.23	-0.57 --	0.549	
High RH	260	35.11	0.31 --	0.752	
Low plus High RH	520	34.67	-0.13 --	0.856	

[a] Transformed from square root scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Difference of adjusted means after transformation to original scale; confidence interval on difference of adjusted means not presented because analysis was performed on square root scale.

[d] P-value is based on difference of means on square root scale.

[e] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 18-65. (Continued)
Analysis of Estradiol (pg/ml)
(Continuous)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

	Current Dioxin Category Mean[a]/(n)			Analysis Results for Log_2 (Current Dioxin + 1)		
Model[b]	Low	Medium	High	R^2	Slope (Std. Error)[c]	p-Value
4	31.86 (295)	31.81 (300)	32.42 (299)	0.002	0.034 (0.027)	0.198
5	31.57 (300)	31.93 (297)	32.59 (297)	0.002	0.028 (0.023)	0.226
6[d]	31.80 (299)	31.96 (297)	32.29 (297)	0.004	0.020 (0.025)	0.418

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

	Current Dioxin Category Adjusted Mean[a]/(n)			Analysis Results for Log_2 (Current Dioxin + 1)			
Model[b]	Low	Medium	High	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
4	35.42 (295)	35.20 (300)	35.49 (299)	0.023	0.024 (0.027)	0.370	AGE (p=0.092) RACE (p<0.001)
5	35.08 (300)	35.27 (297)	35.75 (297)	0.023	0.021 (0.023)	0.362	AGE (p=0.086) RACE (p<0.001)
6[e]	35.59 (299)	35.47 (297)	35.42 (297)	0.027	0.008 (0.025)	0.757	AGE (p=0.057) RACE (p<0.001)

[a] Transformed from square root scale.

[b] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[c] Slope and standard error based on square root of estradiol versus log_2 (current dioxin + 1).

[d] Adjusted for log_2 total lipids.

[e] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 18-66.
Analysis of Estradiol
(Discrete)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Abnormal High**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***952***	***3.8***	***0.95 (0.61,1.46)***	***0.893***
	Comparison	***1,280***	***4.0***		
Officer	Ranch Hand	367	2.7	0.68 (0.31,1.46)	0.414
	Comparison	502	4.0		
Enlisted Flyer	Ranch Hand	162	4.9	1.00 (0.38,2.59)	0.999
	Comparison	202	5.0		
Enlisted Groundcrew	Ranch Hand	423	4.3	1.17 (0.62,2.23)	0.744
	Comparison	576	3.6		

a) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***0.94 (0.61,1.46)***	***0.785***	OCC*AGE (p=0.030) RACE (p=0.110)
Officer	0.67 (0.31,1.44)	0.301	
Enlisted Flyer	1.02 (0.39,2.65)	0.970	
Enlisted Groundcrew	1.17 (0.62,2.33)	0.627	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 18-66. (Continued)
Analysis of Estradiol
(Discrete)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Abnormal High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	174	4.0	1.24 (0.91,1.68)	0.180
Medium	173	2.9		
High	173	5.2		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
520	1.19 (0.85,1.67)	0.308	AGE (p=0.127) RACE (p=0.055)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 18-66. (Continued)
Analysis of Estradiol
(Discrete)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	**n**	**Percent Abnormal High**	**Est. Relative Risk (95% C.I.)[ab]**	**p-Value**
Comparison	1,063	4.5		
Background RH	374	2.7	0.62 (0.31,1.25)	0.180
Low RH	260	3.8	0.82 (0.41,1.64)	0.571
High RH	260	4.2	0.89 (0.45,1.74)	0.729
Low plus High RH	520	4.0	0.85 (0.50,1.44)	0.553

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	**n**	**Adj. Relative Risk (95% C.I.)[ac]**	**p-Value**	**Covariate Remarks**
Comparison	1,063			AGE (p=0.071) RACE (p=0.105)
Background RH	374	0.65 (0.32,1.31)	0.230	
Low RH	260	0.82 (0.41,1.66)	0.590	
High RH	260	0.82 (0.42,1.62)	0.569	
Low plus High RH	520	0.82 (0.49,1.40)	0.469	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 18-66. (Continued)
Analysis of Estradiol
(Discrete)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Abnormal High/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	3.4 (295)	3.0 (300)	4.0 (299)	1.12 (0.88,1.42)	0.370
5	3.0 (300)	3.4 (297)	4.0 (297)	1.08 (0.87,1.33)	0.485
6[c]	3.0 (299)	3.4 (297)	4.0 (297)	1.05 (0.84,1.32)	0.676

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	894	****	****	CURR*OCC (p=0.006) RACE (p=0.017)
5	894	1.08 (0.85,1.39)**	0.527**	CURR*OCC (p=0.017) RACE (p=0.019)
6[d]	893	1.04 (0.80,1.35)**	0.793**	CURR*OCC (p=0.010) RACE (p=0.016)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table N-2-36 for further analysis of this interaction.

**** Log_2 (current dioxin + 1)-by-covariate interaction ($p \leq 0.01$); adjusted relative risk, confidence interval, and p-value not presented; refer to Appendix Table N-2-36 for further analysis of this interaction.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

In Models 2 and 3, no significant associations were found between dioxin and estradiol in the unadjusted and adjusted analyses (Table 18-66(c,d): $p \geq 0.18$ for unadjusted and adjusted analysis). The Model 2 and 3 final adjusted models retained age and race.

The unadjusted analyses for Models 4 through 6 did not reveal a significant association between current dioxin and estradiol (Table 18-66(g): $p \geq 0.37$). The adjusted analysis of Model 4 revealed a highly significant current dioxin-by-occupation interaction (Table 18-66(h): p=0.006). Race also was significant in the final adjusted model. Similarly, Models 5 and 6 revealed significant interactions between current dioxin and occupation (p=0.017 and p=0.010). Race also was significant in these final adjusted models. Removal of the current dioxin-by-occupation in each of these models did not reveal a significant difference between current dioxin and estradiol. Stratified results of each current dioxin-by-occupation interaction in Models 4 through 6 are presented in Appendix Table N-2-36.

Luteinizing Hormone (Continuous)

No significant group differences were shown in the Model 1 unadjusted and adjusted analyses of luteinizing hormone (Table 18-67(a,b): $p > 0.12$ for all analyses). Occupation and age-by-race interaction were significant in the adjusted analysis.

The unadjusted analysis for Model 2 revealed a significant inverse association between initial dioxin and luteinizing hormone in its continuous form (Table 18-67(c): p=0.012, Slope=-0.040). The mean levels of luteinizing hormone adjusted for percent body fat at time of duty in SEA, and change in percent body fat from time of duty in SEA to date of the blood draw for dioxin, are 4.32, 3.97, and 3.66 mIU/ml in the low, medium, and high initial dioxin categories respectively. Adjusting for covariates also revealed a marginally significant inverse relationship between initial dioxin and luteinizing hormone (Table 18-67(d): p=0.061, Adj. Slope=-0.032). Age was retained in the final adjusted model.

In Model 3, the unadjusted and adjusted analysis of luteinizing hormone revealed a significant difference in means between low Ranch Hands and Comparisons (Table 18-67(e): p=0.006 and p=0.019 respectively). In the unadjusted analysis, the mean levels of luteinizing hormone, adjusted for percent body fat at time of duty in SEA, and change in percent body fat from time of duty in SEA to date of the blood draws for dioxin, in the low Ranch Hands category was 4.27 mIU/ml as compared to 3.86 mIU/ml in the Comparison category. Similarly, the adjusted mean levels of luteinizing hormone in the adjusted analysis for the low Ranch Hands and Comparisons categories were 4.15 mIU/ml and 3.82 mIU/ml respectively. Occupation and the age-by-race interaction were retained in the final adjusted model.

The unadjusted analyses for Models 4, 5, and 6 each revealed significant inverse associations between luteinizing hormone and current dioxin (Table 18-67(g): p=0.035, Slope=-0.024 for Model 4; p=0.052, Slope=-0.019 for Model 5; and p=0.035, and Slope= -0.023 for Model 6). After Models 4 through 6 were adjusted for age, the associations between current dioxin and luteinizing hormone were no longer significant (Table 18-67(h): $p > 0.26$).

Table 18-67.
Analysis of Luteinzing Hormone (LH) (mIU/ml)
(Continuous)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	*Ranch Hand*	*952*	*4.02*	*0.14 --*	*0.121*
	Comparison	*1,280*	*3.88*		
Officer	Ranch Hand	367	4.09	0.18 --	0.228
	Comparison	502	3.91		
Enlisted Flyer	Ranch Hand	162	4.11	0.23 --	0.328
	Comparison	202	3.88		
Enlisted Groundcrew	Ranch Hand	423	3.92	0.07 --	0.566
	Comparison	576	3.84		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Group	n	Adj. Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]	Covariate Remarks[d]
All	*Ranch Hand*	*952*	*4.03*	*0.13 --*	0.148	AGE*RACE (p=0.022)
	Comparison	*1,280*	*3.90*			OCC (p=0.122)
Officer	Ranch Hand	367	3.94	0.15 --	0.288	
	Comparison	502	3.79			
Enlisted Flyer	Ranch Hand	162	4.06	0.21 --	0.347	
	Comparison	202	3.85			
Enlisted Groundcrew	Ranch Hand	423	4.12	0.08 --	0.547	
	Comparison	576	4.04			

[a] Transformed from the natural logarithm scale.

[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.

[c] P-values based on difference of means on natural logarithm scale.

[d] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 18-67. (Continued)
Analysis of Luteinizing Hormone (LH) (mIU/ml)
(Continuous)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	174	4.32	4.32	0.025	-0.040 (0.016)	0.012
Medium	173	3.96	3.97			
High	173	3.66	3.66			

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED						
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[d]			
Initial Dioxin	n	Adj. Mean[ad]	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
Low	174	4.27	0.031	-0.032 (0.017)	0.061	AGE (p=0.074)
Medium	173	3.96				
High	173	3.71				

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Slope and standard error based on natural logarithm of luteinizing hormone versus $\log_2$ (initial dioxin).

[d] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 18-67. (Continued)
Analysis of Luteinizing Hormone (LH) (mIU/ml)
(Continuous)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,063	3.86	3.86		
Background RH	374	4.03	4.00	0.14 --	0.265
Low RH	260	4.29	4.27	0.41 --	0.006
High RH	260	3.68	3.72	-0.14 --	0.310
Low plus High RH	520	3.97	3.99	0.13 --	0.265

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Mean[ae]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]	Covariate Remarks
Comparison	1,063	3.82			AGE*RACE (p=0.014) OCC (p=0.076)
Background RH	374	3.94	0.12 --	0.322	
Low RH	260	4.15	0.33 --	0.019	
High RH	260	3.73	-0.09 --	0.516	
Low plus High RH	520	4.00	0.18 --	0.286	

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Difference of adjusted means after transformation to original scale; confidence interval on difference of adjusted means not presented because analysis was performed on natural logarithm scale.

[d] P-value is based on difference of means on natural logarithm scale.

[e] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤10 ppt.
Background (Ranch Hand): Current Dioxin ≤10 ppt.
Low (Ranch Hand): Current Dioxin >10 ppt, 10 ppt < Initial Dioxin ≤143 ppt.
High (Ranch Hand): Current Dioxin >10 ppt, Initial Dioxin >143 ppt.

Table 18-67. (Continued)
Analysis of Luteinizing Hormone (LH) (mIU/ml)
(Continuous)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED						
	Current Dioxin Category Mean[a]/(n)			Analysis Results for Log_2 (Current Dioxin + 1)		
Model[b]	Low	Medium	High	R^2	Slope (Std. Error)[c]	p-Value
4	4.05 (295)	4.20 (300)	3.76 (299)	0.005	-0.024 (0.012)	0.035
5	4.06 (300)	4.15 (297)	3.79 (297)	0.004	-0.019 (0.010)	0.052
6[d]	4.08 (299)	4.15 (297)	3.77 (297)	0.005	-0.023 (0.011)	0.035

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED							
	Current Dioxin Category Adjusted Mean[a]/(n)			Analysis Results for Log_2 (Current Dioxin + 1)			
Model[b]	Low	Medium	High	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
4	4.01 (295)	4.13 (300)	3.85 (299)	0.027	-0.013 (0.012)	0.264	AGE ($p<0.001$)
5	4.02 (300)	4.09 (297)	3.88 (297)	0.027	-0.011 (0.010)	0.280	AGE ($p<0.001$)
6[e]	4.03 (299)	4.09 (297)	3.87 (297)	0.027	-0.012 (0.011)	0.264	AGE ($p<0.001$)

[a] Transformed from natural logarithm scale.

[b] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[c] Slope and standard error based on natural logarithm of luteinizing hormone versus log_2 (current dioxin + 1).

[d] Adjusted for log_2 total lipids.

[e] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Luteinizing Hormone (Discrete)

Results from the Model 1 analyses of luteinizing hormone in its discrete form were nonsignificant (Table 18-68(a,b): $p>0.16$ for all analyses). Age was retained in the adjusted analysis.

The unadjusted analysis for Model 2 did not reveal a significant relationship between initial dioxin and luteinizing hormone in its discrete form (Table 18-68(c): $p=0.202$). After adjusting for age, the association between initial dioxin and luteinizing hormone became significant (Table 18-68(d): $p=0.042$, Adj. RR=1.92).

In Model 3, the unadjusted and adjusted analyses of luteinizing hormone revealed no significant differences between the Ranch Hand categories and Comparisons (Table 18-68(e,f): $p>0.15$ for all contrasts). Age was retained in the adjusted analysis.

The unadjusted and adjusted analyses for Models 4 through 6 did not reveal any significant associations between luteinizing hormone and current dioxin (Table 18-68(g,h): $p>0.28$ for unadjusted and adjusted analyses). In each of Models 4, 5, and 6, the final adjusted model contained age. In Model 6, occupation also was retained in the adjusted model.

Follicle Stimulating Hormone (Continuous)

Ranch Hands did not differ significantly from Comparisons in the Model 1 unadjusted and adjusted analyses of follicle stimulating hormone (Table 18-69(a,b): $p\geq0.33$ for all analyses). Age and occupation were retained in the adjusted analysis.

The unadjusted and adjusted analyses for Model 2 did not show a significant relationship between follicle stimulating hormone in its continuous form and initial dioxin (Table 18-69(c,d): $p>0.10$ for unadjusted and adjusted analyses). Age was retained in the final adjusted model.

The unadjusted analysis of Model 3 revealed a marginally significant difference in means between the low Ranch Hands and Comparisons (Table 18-69(e): $p=0.079$). The mean level of follicle stimulating hormone, adjusted for percent body fat at time of duty in SEA and percent body fat from time of duty in SEA to the date of the blood draw for dioxin, was 4.67 mIU/ml in the background Ranch Hand category as compared to 4.30 mIU/ml in the Comparison group. Adjusting for covariates in Model 3 did not reveal a significant association between follicle stimulating hormone and categorized dioxin (Table 18-69(f): $p>0.18$ for all adjusted contrasts). Age and race were significant in the final adjusted model.

The unadjusted and adjusted analyses for Models 4, 5, and 6 did not reveal any significant associations between current dioxin and follicle stimulating hormone (Table 18-69(g,h): $p>0.22$ for unadjusted and adjusted analyses). Age was significant in each of the final adjusted models.

Table 18-68.
Analysis of Luteinizing Hormone (LH)
(Discrete)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Abnormal High**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***952***	***1.7***	***0.82 (0.44,1.55)***	***0.656***
	Comparison	***1,280***	***2.0***		
Officer	Ranch Hand	367	1.4	0.48 (0.17,1.35)	0.236
	Comparison	502	2.8		
Enlisted Flyer	Ranch Hand	162	2.5	1.25 (0.31,5.09)	0.999
	Comparison	202	2.0		
Enlisted Groundcrew	Ranch Hand	423	1.7	1.20 (0.43,3.32)	0.938
	Comparison	576	1.4		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks**[a]
All	***0.81 (0.43,1.54)***	***0.519***	AGE (p<0.001)
Officer	0.48 (0.17,1.35)	0.165	
Enlisted Flyer	1.22 (0.30,5.01)	0.785	
Enlisted Groundcrew	1.17 (0.41,3.34)	0.765	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 18-68. (Continued)
Analysis of Luteinizing Hormone (LH)
(Discrete)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Abnormal High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	174	1.2	1.46 (0.83,2.57)	0.202
Medium	173	1.2		
High	173	1.2		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
520	1.92 (1.04,3.52)	0.042	AGE ($p<0.001$)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 18-68. (Continued)
Analysis of Luteinizing Hormone (LH)
(Discrete)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Abnormal High	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,063	2.2		
Background RH	374	2.4	1.10 (0.50,2.42)	0.811
Low RH	260	1.2	0.50 (0.15,1.69)	0.267
High RH	260	1.2	0.53 (0.16,1.78)	0.303
Low plus High RH	520	1.2	0.51 (0.21,1.28)	0.153

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,063			AGE ($p<0.001$)
Background RH	374	0.99 (0.44,2.21)	0.978	
Low RH	260	0.45 (0.13,1.56)	0.208	
High RH	260	0.74 (0.22,2.58)	0.640	
Low plus High RH	520	0.56 (0.22,1.43)	0.226	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤10 ppt.
Background (Ranch Hand): Current Dioxin ≤10 ppt.
Low (Ranch Hand): Current Dioxin >10 ppt, 10 ppt < Initial Dioxin ≤143 ppt.
High (Ranch Hand): Current Dioxin >10 ppt, Initial Dioxin >143 ppt.

Table 18-68. (Continued)
Analysis of Luteinizing Hormone (LH)
(Discrete)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Abnormal High/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	2.0 (295)	1.7 (300)	1.3 (299)	0.87 (0.60,1.26)	0.454
5	2.3 (300)	1.0 (297)	1.7 (297)	0.92 (0.68,1.24)	0.576
6[c]	2.3 (299)	1.0 (297)	1.7 (297)	0.86 (0.62,1.18)	0.356

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	894	0.97 (0.64,1.48)	0.883	AGE (p<0.001)
5	894	1.00 (0.70,1.41)	0.982	AGE (p<0.001)
6[d]	893	0.81 (0.56,1.17)	0.281	AGE (p<0.001) OCC (p=0.141)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 18-69.
Analysis of Follicle Stimulating Hormone (FSH) (mIU/ml)
(Continuous)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***952***	***4.41***	***0.08 --***	***0.535***
	Comparison	***1,280***	***4.33***		
Officer	Ranch Hand	367	4.66	0.12 --	0.581
	Comparison	502	4.54		
Enlisted Flyer	Ranch Hand	162	4.63	0.33 --	0.330
	Comparison	202	4.30		
Enlisted Groundcrew	Ranch Hand	423	4.12	-0.04 --	0.812
	Comparison	576	4.16		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Group	n	Adj. Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]	Covariate Remarks[d]
All	***Ranch Hand***	***952***	***4.37***	***0.06 --***	0.631	AGE ($p<0.001$)
	Comparison	***1,280***	***4.31***			OCC ($p=0.131$)
Officer	Ranch Hand	367	4.28	0.07 --	0.717	
	Comparison	502	4.21			
Enlisted Flyer	Ranch Hand	162	4.42	0.29 --	0.336	
	Comparison	202	4.13			
Enlisted Groundcrew	Ranch Hand	423	4.49	-0.04 --	0.838	
	Comparison	576	4.53			

[a] Transformed from the natural logarithm scale.

[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.

[c] P-values based on difference of means on natural logarithm scale.

[d] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 18-69. (Continued)
Analysis of Follicle Stimulating Hormone (FSH) (mIU/ml) (Continuous)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	174	4.95	4.95	0.009	-0.035 (0.022)	0.109
Medium	173	4.24	4.25			
High	173	4.08	4.06			

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[d]			
Initial Dioxin	n	Adj. Mean[ad]	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
Low	174	4.74	0.053	-0.003 (0.023)	0.903	AGE ($p<0.001$)
Medium	173	4.21				
High	173	4.28				

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Slope and standard error based on natural logarithm of follicle stimulating hormone versus $\log_2$ (initial dioxin).

[d] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 18-69. (Continued)
Analysis of Follicle Stimulating Hormone (FSH) (mIU/ml)
(Continuous)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,063	4.30	4.30		
Background RH	374	4.42	4.43	0.13 --	0.465
Low RH	260	4.71	4.67	0.37 --	0.079
High RH	260	4.12	4.13	-0.17 --	0.377
Low plus High RH	520	4.41	4.39	0.09 --	0.575

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Mean[ae]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]	Covariate Remarks
Comparison	1,063	4.10			AGE ($p<0.001$) RACE ($p=0.089$)
Background RH	374	4.08	-0.02 --	0.923	
Low RH	260	4.35	0.25 --	0.187	
High RH	260	4.18	0.08 --	0.644	
Low plus High RH	520	4.27	0.17 --	0.249	

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Difference of adjusted means after transformation to original scale; confidence interval on difference of adjusted means not presented because analysis was performed on natural logarithm scale.

[d] P-value is based on difference of means on natural logarithm scale.

[e] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 18-69. (Continued)
Analysis of Follicle Stimulating Hormone (FSH) (mIU/ml)
(Continuous)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED						
	Current Dioxin Category Mean[a]/(n)			Analysis Results for Log_2 (Current Dioxin + 1)		
Model[b]	Low	Medium	High	R^2	Slope (Std. Error)[c]	p-Value
4	4.42 (295)	4.75 (300)	4.09 (299)	0.001	-0.014 (0.016)	0.383
5	4.44 (300)	4.62 (297)	4.17 (297)	<0.001	-0.006 (0.013)	0.640
6[d]	4.55 (299)	4.63 (297)	4.08 (297)	0.004	-0.018 (0.014)	0.226

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED							
	Current Dioxin Category Adjusted Mean[a]/(n)			Analysis Results for Log_2 (Current Dioxin + 1)			
Model[b]	Low	Medium	High	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
4	4.32 (295)	4.58 (300)	4.33 (299)	0.066	0.012 (0.016)	0.423	AGE (p<0.001)
5	4.36 (300)	4.47 (297)	4.40 (297)	0.066	0.013 (0.013)	0.317	AGE (p<0.001)
6[e]	4.43 (299)	4.48 (297)	4.34 (297)	0.067	0.006 (0.014)	0.664	AGE (p<0.001)

[a] Transformed from natural logarithm scale.

[b] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for $\log_2$ total lipids.

[c] Slope and standard error based on natural logarithm of follicle stimulating hormone versus $\log_2$ (current dioxin + 1).

[d] Adjusted for $\log_2$ total lipids.

[e] Adjusted for $\log_2$ total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Follicle Stimulating Hormone (Discrete)

In both the unadjusted and adjusted Model 1 analyses of follicle stimulating hormone, Ranch Hands in the officer stratum possessed a significantly greater percentage of abnormalities than Comparisons, although the unadjusted contrast was only marginally significant (Table 18-70(a,b): p=0.062, Est. RR=1.85 for the unadjusted analysis and p=0.046, Adj. RR=1.86 for the adjusted analysis). All other group contrasts were nonsignificant (p>0.21). Age was the only covariate retained in the adjusted analysis.

The unadjusted and adjusted analyses of Models 2 through 6 did not reveal any significant associations between dioxin and follicle stimulating hormone in its categorized form (Table 18-70(c-h): p>0.15 for all unadjusted and adjusted analyses). Adjusting for covariates in Model 2 revealed a significant age-by-race interaction. Age was significant in the final adjusted model for Models 3 through 6.

Longitudinal Analysis

Longitudinal analyses were conducted on the composite diabetes indicator, TSH, fasting glucose, 2-hour postprandial glucose, and total testosterone to examine whether changes across time differed with respect to group membership (Model 1), initial dioxin (Model 2), and categorized dioxin (Model 3). Models 4, 5, and 6 were not examined in longitudinal analyses because current dioxin, the measure of exposure in these models, changes over time and is not available for all participants for 1982, 1985, or 1992. The longitudinal analyses were conducted on TSH, fasting glucose, 2-hour postprandial glucose, and total testosterone in both continuous and discrete forms. The longitudinal analyses of 2-hour postprandial glucose were restricted to nondiabetics; the other longitudinal analyses were conducted on all participants with available data.

The longitudinal analysis for the continuous variables (TSH, fasting glucose, 2-hour postprandial glucose, and total testosterone) examined the paired difference between the measurements from 1982 and 1992. Each of the three models used in the longitudinal analysis were adjusted for age and the dependent variable measured in 1982. The analyses of Models 2 and 3 also were adjusted for percent body fat at time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

The longitudinal analyses for the discrete variables (composite diabetes indicator, TSH, fasting glucose, 2-hour postprandial glucose, and total testosterone) examined relative risks at the 1992 examination for participants who were classified as normal at the 1982 examination. Participants considered abnormal in 1982 were excluded because the focus of the analyses was on investigating the temporal effects of dioxin during the period between 1982 and 1992. Participants considered abnormal in 1982 were already abnormal before this period; consequently, only participants considered normal at the 1982 examination were considered to be at risk when the effects of dioxin over time were explored. The rate of abnormalities under this restriction approximates an incidence rate between 1982 and 1992. All three models were adjusted for age; Models 2 and 3 also were adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

Table 18-70.
Analysis of Follicle Stimulating Hormone (FSH)
(Discrete)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Abnormal High**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***950***	***4.9***	***1.30 (0.87,1.96)***	***0.241***
	Comparison	***1,277***	***3.8***		
Officer	Ranch Hand	365	7.1	1.85 (1.02,3.37)	0.062
	Comparison	502	4.0		
Enlisted Flyer	Ranch Hand	162	6.2	1.26 (0.51,3.11)	0.782
	Comparison	202	5.0		
Enlisted Groundcrew	Ranch Hand	423	2.6	0.78 (0.37,1.65)	0.652
	Comparison	573	3.3		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***1.30 (0.86,1.98)***	***0.217***	AGE (p<0.001)
Officer	1.86 (1.01,3.42)	0.046	
Enlisted Flyer	1.23 (0.50,3.08)	0.625	
Enlisted Groundcrew	0.77 (0.36,1.66)	0.502	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 18-70. (Continued)
Analysis of Follicle Stimulating Hormone (FSH)
(Discrete)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Abnormal High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	174	6.3	0.97 (0.71,1.32)	0.822
Medium	173	4.0		
High	173	3.5		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
520	1.15 (0.83,1.60)	0.408	AGE*RACE (p=0.009)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 18-70. (Continued)
Analysis of Follicle Stimulating Hormone (FSH)
(Discrete)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Percent Abnormal High	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,063	3.7		
Background RH	374	5.3	1.44 (0.82,2.52)	0.204
Low RH	260	5.8	1.56 (0.84,2.89)	0.159
High RH	260	3.5	0.96 (0.46,2.02)	0.918
Low plus High RH	520	4.6	1.27 (0.75,2.14)	0.378

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,063			AGE ($p<0.001$)
Background RH	374	1.32 (0.75,2.32)	0.341	
Low RH	260	1.47 (0.79,2.75)	0.230	
High RH	260	1.25 (0.58,2.66)	0.569	
Low plus High RH	520	1.38 (0.81,2.35)	0.242	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 18-70. (Continued)
Analysis of Follicle Stimulating Hormone (FSH)
(Discrete)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Abnormal High/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	4.4 (295)	7.0 (300)	3.3 (299)	0.97 (0.79,1.20)	0.787
5	5.0 (300)	5.7 (297)	4.0 (297)	1.00 (0.84,1.20)	0.973
6[c]	5.0 (299)	5.7 (297)	4.0 (297)	0.96 (0.79,1.16)	0.653

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	894	1.07 (0.85,1.35)	0.543	AGE ($p<0.001$)
5	894	1.09 (0.89,1.32)	0.409	AGE ($p<0.001$)
6[d]	893	1.05 (0.85,1.30)	0.676	AGE ($p<0.001$)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = $\leq$ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = $\leq$ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Medical Records and Laboratory Variable

Composite Diabetes Indicator

No significant results were disclosed in the longitudinal analyses of composite diabetes indicator for Models 1, 2, and 3 (Table 18-71(a-c): p>0.25 for all analyses).

Laboratory Variables

Thyroid Stimulating Hormone (TSH) (Continuous)

Thyroid stimulating hormone (TSH) group differences of examination mean change (from 1982 to 1992) overall by occupation and within the officer and enlisted groundcrew strata were nonsignificant (Table 18-72(a): p>0.53 for each analysis). The enlisted flyer stratum displayed a marginally significant difference of examination mean change (p=0.082, Diff. of Exam. Mean Change=0.54).

The Model 2 longitudinal analysis was nonsignificant (Table 18-72(b): p=0.909). Also, each Model 3 difference of examination mean change between Ranch Hands and Comparisons was nonsignificant, except for the high Ranch Hand difference (Table 18-72(c): p>0.35 for each difference). Results were marginally significant for the difference between high Ranch Hands and Comparisons. High Ranch Hands exhibited a smaller decrease in examination means from 1982 to 1992 than Comparisons (Table 18-72(c): p=0.088, Diff. of Exam. Mean Change=0.28).

Thyroid Stimulating Hormone (Discrete)

The Model 1 Ranch Hand versus Comparison contrast within the officer strata displayed a marginally significant difference in thyroid stimulating hormone abnormality rates (Table 18-73(a): p=0.090, Adj. RR=0.41). Conditioned on normality in 1982, Comparisons exhibited a higher percentage of abnormalities in 1992 than Ranch Hands. All other Model 1 contrasts were nonsignificant, as well as all remaining Model 2 and Model 3 analyses (Table 18-73(a-c): p>0.11). All analyses were restricted to participants who had normal thyroid stimulating hormone levels in 1982.

Fasting Glucose (All Participants—Continuous)

The Model 1 analysis of fasting glucose did not reveal a significant overall difference of examination mean change between Ranch Hands and Comparisons (Table 18-74(a): p=0.369). Analyses conducted within each occupational strata also were nonsignificant (p>0.18 for each analysis). The Model 2 analysis displayed a marginally significant positive association between initial dioxin and the difference between fasting glucose in 1992 and fasting glucose in 1982 (Table 18-74(b): p=0.072, Adj. Slope=0.011). All Model 3 contrasts between the Ranch Hand categories and Comparisons were nonsignificant from the analysis of fasting glucose in all participants (Table 18-74(c): p>0.27 for all analyses).

Table 18-71.
Longitudinal Analysis of Composite Diabetes Indicator

a) MODEL 1: RANCH HANDS VS. COMPARISONS					
		Percent Abnormal/(n) Examination			
Occupational Category	Group	1982	1985	1987	1992
All	*Ranch Hand*	*4.1*	*8.8*	*10.3*	*15.6*
		(898)	*(877)*	*(866)*	*(898)*
	Comparison	*3.9*	*9.1*	*10.3*	*14.9*
		(1,060)	*(1,035)*	*(1,029)*	*(1,060)*
Officer	Ranch Hand	4.1	9.3	10.0	15.7
		(338)	(333)	(331)	(338)
	Comparison	2.5	7.1	8.2	12.4
		(404)	(395)	(391)	(404)
Enlisted Flyer	Ranch Hand	4.4	7.6	8.4	15.7
		(159)	(157)	(155)	(159)
	Comparison	5.7	10.5	12.1	17.7
		(175)	(172)	(173)	(175)
Enlisted Groundcrew	Ranch Hand	4.0	8.8	11.3	15.5
		(401)	(387)	(380)	(401)
	Comparison	4.4	10.3	11.4	16.0
		(481)	(468)	(465)	(481)

		Normal in 1982			
Occupational Category	Group	n in 1992	Percent Abnormal in 1992	Adj. Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*861*	*12.0*	*1.07 (0.81,1.43)*	*0.629*
	Comparison	*1,019*	*11.5*		
Officer	Ranch Hand	324	12.0	1.25 (0.78,2.01)	0.357
	Comparison	394	10.2		
Enlisted Flyer	Ranch Hand	152	11.8	0.92 (0.47,1.81)	0.808
	Comparison	165	12.7		
Enlisted Groundcrew	Ranch Hand	385	12.0	1.03 (0.67,1.57)	0.895
	Comparison	460	12.2		

[a] Relative risk, confidence interval, and p-values are in reference to a contrast of 1982 and 1992 results; results adjusted for age in 1992.

Note: Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations. Statistical analyses are based only on participants who did not have diabetes or a 2-hour postprandial glucose level >200 mg/dl in 1982 (see Chapter 7, Statistical Methods).

Table 18-71. (Continued)
Longitudinal Analysis of Composite Diabetes Indicator

b) MODEL 2: RANCH HANDS — INITIAL DIOXIN				
	Percent Abnormal/(n) Examination			
Initial Dioxin	1982	1985	1987	1992
Low	4.8 (166)	9.8 (163)	10.8 (166)	18.7 (166)
Medium	4.2 (168)	11.0 (163)	10.4 (163)	18.5 (168)
High	7.1 (168)	13.3 (166)	16.1 (162)	20.2 (168)

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
	Normal in 1982			
Initial Dioxin	n in 1992	Percent Abnormal in 1992	Adj. Relative Risk (95% C.I.)	p-Value
Low	158	14.6	1.10 (0.89,1.36)	0.375
Medium	161	14.9		
High	156	14.1		

[a] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to date of blood draw for dioxin, and age in 1992.

[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.
Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations. Statistical analyses are based only on participants who did not have diabetes or a 2-hour postprandial glucose level >200 Mg/dl in 1982 (see Chapter 7, Statistical Methods).

Table 18-71. (Continued)
Longitudinal Analysis of Composite Diabetes Indicator

c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY				
	Percent Abnormal/(n) Examination			
Dioxin Category	1982	1985	1987	1992
Comparison	3.7 (914)	8.7 (902)	10.1 (902)	14.9 (914)
Background RH	2.9 (341)	5.9 (338)	7.5 (334)	11.7 (341)
Low RH	4.4 (248)	11.2 (242)	11.4 (246)	19.7 (248)
High RH	6.3 (254)	11.6 (250)	13.5 (245)	18.5 (254)
Low plus High RH	5.4 (502)	11.4 (492)	12.4 (491)	19.1 (502)

	Normal in 1982			
Dioxin Category	n in 1992	Percent Abnormal in 1992	Adj. Relative Risk (95% C.I.)	p-Value
Comparison	880	11.6		
Background RH	331	9.1	0.90 (0.57,1.40)	0.633
Low RH	237	16.0	1.28 (0.83,1.98)	0.255
High RH	238	13.0	1.15 (0.72,1.83)	0.566
Low plus High RH	475	14.5	1.22 (0.86,1.73)	0.268

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to date of blood draw for dioxin, and age in 1992.

Note: RH = Ranch Hand.
Comparison: Current Dioxin $\leq$10 ppt.
Background (Ranch Hand): Current Dioxin $\leq$10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt. < Initial Dioxin $\leq$143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.
Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations. Statistical analyses are based only on participants who did not have diabetes or a 2-hour postprandial glucose level >200 mg/dl in 1982 (see Chapter 7, Statistical Methods).

Table 18-72.
Longitudinal Analysis of Thyroid Stimulating Hormone (μIU/ml) (TSH)
(Continuous)

a) MODEL 1: RANCH HANDS VS. COMPARISONS								
		Mean/(n) Examination						
Occupational Category	Group	1982	1985	1987	1992	Exam. Mean Change[a]	Difference of Exam. Mean Change	p-Value[b]
All	*Ranch Hand*	*3.89 (880)*	*1.40 (857)*	*1.12 (845)*	*2.11 (880)*	*-1.78*	*0.04*	*0.543*
	Comparison	*3.75 (1,024)*	*1.31 (1,001)*	*1.04 (998)*	*1.92 (1,024)*	*-1.82*		
Officer	Ranch Hand	4.00 (329)	1.51 (323)	1.21 (321)	2.30 (329)	-1.70	0.04	0.640
	Comparison	3.71 (384)	1.30 (376)	1.05 (373)	1.97 (384)	-1.74		
Enlisted Flyer	Ranch Hand	3.70 (155)	1.30 (153)	1.01 (149)	2.21 (155)	-1.49	0.54	0.082
	Comparison	4.03 (171)	1.39 (168)	1.15 (170)	2.00 (171)	-2.03		
Enlisted Groundcrew	Ranch Hand	3.86 (396)	1.34 (381)	1.09 (375)	1.91 (396)	-1.95	-0.14	0.534
	Comparison	3.68 (469)	1.27 (457)	1.00 (455)	1.86 (469)	-1.81		

[a] Difference between 1992 and 1982 examination means.

[b] Results adjusted for thyroid stimulating hormone in 1982 and age in 1992.

Note: Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1982, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1985, 1987, and 1992 examinations.

Table 18-72. (Continued)
Longitudinal Analysis of Thyroid Stimulating Hormone (μIU/ml) (TSH) (Continuous)

b) MODEL 2: RANCH HANDS — INITIAL DIOXIN						
	Initial Dioxin Category Summary Statistics Mean/(n) Examination				Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	1982	1985	1987	1992	Adj. Slope (Std. Error)	p-Value
Low	3.82 (162)	1.32 (159)	1.05 (160)	1.86 (162)	-0.017 (0.151)	0.909
Medium	3.78 (167)	1.51 (161)	1.20 (162)	2.18 (167)		
High	3.99 (163)	1.41 (161)	1.15 (157)	2.45 (163)		

[a] Results based on difference between thyroid stimulating hormone in 1992 and thyroid stimulating hormone in 1982 versus $\log_2$ (initial dioxin); results adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to date of blood draw for dioxin, thyroid stimulating hormone in 1982, and age in 1992.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.
Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1982, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1985, 1987, and 1992 examinations.

Table 18-72. (Continued)
Longitudinal Analysis of Thyroid Stimulating Hormone (μIU/ml) (TSH) (Continuous)

c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY							
	Mean/(n) Examination						
Dioxin Category	1982	1985	1987	1992	Exam. Mean Change[a]	Difference of Exam. Mean Change[b]	p-Value[c]
Comparison	3.75 (883)	1.30 (872)	1.05 (873)	1.93 (883)	-1.81		
Background RH	3.94 (333)	1.39 (330)	1.12 (325)	2.10 (333)	-1.85	-0.04	0.893
Low RH	3.77 (243)	1.34 (237)	1.07 (240)	1.90 (243)	-1.87	-0.06	0.791
High RH	3.95 (249)	1.50 (244)	1.20 (239)	2.42 (249)	-1.53	0.28	0.088
Low plus High RH	3.86 (492)	1.42 (481)	1.13 (479)	2.16 (492)	-1.70	0.11	0.357

[a] Difference between 1992 and 1982 examination means.

[b] Difference between Ranch Hand dioxin category and Comparison category.

[c] Results adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to date of blood draw for dioxin, thyroid stimulating hormone in 1982, and age in 1992.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.
Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1982, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1985, 1987, and 1992 examinations.

Table 18-73.
Longitudinal Analysis of Thyroid Stimulating Hormone (TSH)
(Discrete)

a) MODEL 1: RANCH HANDS VS. COMPARISONS					
		Percent Abnormal High/(n) Examination			
Occupational Category	**Group**	**1982**	**1985**	**1987**	**1992**
All	***Ranch Hand***	***0.7*** ***(880)***	***2.1*** ***(857)***	***2.0*** ***(845)***	***2.3*** ***(880)***
	Comparison	***0.5*** ***(1,024)***	***1.9*** ***(1,001)***	***1.6*** ***(998)***	***2.3*** ***(1,024)***
Officer	Ranch Hand	0.9 (329)	2.5 (323)	2.5 (321)	2.4 (329)
	Comparison	0.3 (384)	1.9 (376)	1.6 (373)	3.7 (384)
Enlisted Flyer	Ranch Hand	0.7 (155)	2.0 (153)	2.0 (149)	2.6 (155)
	Comparison	1.2 (171)	1.8 (168)	1.2 (170)	1.2 (171)
Enlisted Groundcrew	Ranch Hand	0.5 (396)	1.8 (381)	1.6 (375)	2.0 (396)
	Comparison	0.4 (469)	2.0 (457)	1.8 (455)	1.7 (469)

		Normal in 1982			
Occupational Category	**Group**	**n in 1992**	**Percent Abnormal High in 1992**	**Adj. Relative Risk (95% C.I.)[a]**	**p-Value[a]**
All	***Ranch Hand***	***874***	***1.7***	***0.80 (0.41,1.55)***	***0.503***
	Comparison	***1,019***	***2.2***		
Officer	Ranch Hand	326	1.5	0.41 (0.15,1.15)	0.090
	Comparison	383	3.7		
Enlisted Flyer	Ranch Hand	154	2.0	3.36 (0.35,32.36)	0.294
	Comparison	169	0.6		
Enlisted Groundcrew	Ranch Hand	394	1.8	1.21 (0.42,3.49)	0.719
	Comparison	467	1.5		

[a] Relative risk, confidence interval, and p-values are in reference to a contrast of 1982 and 1992 results; results adjusted for age in 1992.

Note: Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations. Statistical analyses are based only on participants who had a normal thyroid stimulating hormone level in 1982 (see Chapter 7, Statistical Methods).

Table 18-73. (Continued)
Longitudinal Analysis of Thyroid Stimulating Hormone (TSH)
(Discrete)

b) MODEL 2: RANCH HANDS — INITIAL DIOXIN				
	Percent Abnormal High/(n) Examination			
Initial Dioxin	1982	1985	1987	1992
Low	0.0 (162)	0.6 (159)	0.6 (160)	0.6 (162)
Medium	0.6 (167)	2.5 (161)	1.9 (162)	1.2 (167)
High	1.2 (163)	2.5 (161)	3.2 (157)	4.9 (163)

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
	Normal in 1982			
Initial Dioxin	n in 1992	Percent Abnormal High in 1992	Adj. Relative Risk (95% C.I.)[b]	p-Value
Low	162	0.6	1.48 (0.92,2.38)	0.116
Medium	166	1.2		
High	161	3.7		

[a] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to date of blood draw for dioxin, and age in 1992.

[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.
Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations. Statistical analyses are based only on participants who had a normal thyroid stimulating hormone level in 1982 (see Chapter 7, Statistical Methods).

Table 18-73. (Continued)
Longitudinal Analysis of Thyroid Stimulating Hormone (TSH)
(Discrete)

c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY				
	Percent Abnormal/(n) Examination			
Dioxin Category	**1982**	**1985**	**1987**	**1992**
Comparison	0.5 (883)	2.0 (872)	1.6 (873)	2.5 (883)
Background RH	0.9 (333)	2.7 (330)	2.5 (325)	2.7 (333)
Low RH	0.0 (243)	0.8 (237)	0.8 (240)	0.8 (243)
High RH	1.2 (249)	2.9 (244)	2.9 (239)	3.6 (249)
Low plus High RH	0.6 (492)	1.9 (481)	1.9 (479)	2.2 (492)

	Normal in 1982			
Dioxin Category	**n in 1992**	**Percent Abnormal in 1992**	**Adj. Relative Risk (95% C.I.)[ab]**	**p-Value[b]**
Comparison	879	2.3		
Background RH	330	1.8	0.69 (0.27,1.76)	0.437
Low RH	243	0.8	0.35 (0.08,1.50)	0.155
High RH	246	2.9	1.54 (0.63,3.75)	0.346
Low plus High RH	489	1.8	0.87 (0.39,1.93)	0.723

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to date of blood draw for dioxin, and age in 1992.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤10 ppt.
Background (Ranch Hand): Current Dioxin ≤10 ppt.
Low (Ranch Hand): Current Dioxin >10 ppt, 10 ppt < Initial Dioxin ≤143 ppt.
High (Ranch Hand): Current Dioxin >10 ppt, Initial Dioxin > 143 ppt.
Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations. Statistical analyses are based only on participants who had a normal thyroid stimulating hormone level in 1982 (see Chapter 7, Statistical Methods).

Table 18-74.
Longitudinal Analysis of Fasting Glucose (mg/dl) (All Participants) (Continuous)

a) MODEL 1: RANCH HANDS VS. COMPARISONS								
		Mean[a]/(n) Examination						
Occupational Category	Group	1982	1985	1987	1992	Exam. Mean Change[b]	Difference of Exam. Mean Change	p-Value[c]
All	*Ranch Hand*	*97.66 (899)*	*99.01 (877)*	*100.61 (867)*	*104.44 (899)*	*6.78*	*-1.30*	*0.369*
	Comparison	*96.61 (1,060)*	*98.29 (1,037)*	*100.22 (1,033)*	*104.69 (1,060)*	*8.09*		
Officer	Ranch Hand	98.54 (338)	100.46 (333)	101.81 (331)	105.45 (338)	6.91	-0.51	0.947
	Comparison	97.19 (403)	97.99 (395)	100.33 (391)	104.61 (403)	7.42		
Enlisted Flyer	Ranch Hand	98.24 (159)	98.63 (157)	100.53 (154)	103.84 (159)	5.60	-2.50	0.185
	Comparison	98.92 (175)	100.23 (172)	101.71 (174)	107.03 (175)	8.11		
Enlisted Groundcrew	Ranch Hand	96.69 (402)	97.92 (387)	99.61 (382)	103.83 (402)	7.14	-1.49	0.587
	Comparison	95.30 (482)	97.84 (470)	99.58 (468)	103.92 (482)	8.63		

[a] Transformed from natural logarithm scale.

[b] Difference between 1992 and 1982 examination means after transformation to original scale.

[c] P-value is based on analysis of natural logarithm of fasting glucose; results adjusted for natural logarithm of fasting glucose in 1982 and age in 1992.

Note: Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1982, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations.

Table 18-74. (Continued)
Longitudinal Analysis of Fasting Glucose (mg/dl) (All Participants) (Continuous)

b) MODEL 2: RANCH HANDS — INITIAL DIOXIN						
	Initial Dioxin Category Summary Statistics Mean/(n) Examination				Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	1982	1985	1987	1992	Adj. Slope (Std. Error)	p-Value
Low	97.66 (166)	99.78 (163)	101.41 (165)	104.73 (166)	0.011 (0.006)	0.072
Medium	98.89 (168)	99.81 (162)	101.06 (164)	104.74 (168)		
High	98.97 (168)	101.22 (166)	104.35 (162)	109.29 (168)		

[a] Transformed from natural logarithm scale.

[b] Results based on difference between natural logarithm of fasting glucose in 1992 and natural logarithm of fasting glucose in 1982 versus $\log_2$ (initial dioxin); results adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to date of blood draw for dioxin, natural logarithm of 1982 fasting glucose, and age in 1992.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.
Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1982, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations.

Table 18-74. (Continued)
Longitudinal Analysis of Fasting Glucose (mg/dl) (All Participants)
(Continuous)

c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY							
	Mean[a]/(n) Examination						
Dioxin Category	1982	1985	1987	1992	Exam. Mean Change[b]	Difference of Exam. Mean Change[c]	p-Value[d]
Comparison	96.42 (914)	98.27 (903)	100.20 (904)	104.39 (914)	7.98		
Background RH	97.16 (342)	97.66 (339)	98.68 (335)	102.45 (342)	5.28	-2.69	0.384
Low RH	98.28 (248)	100.21 (242)	101.25 (246)	105.13 (248)	6.84	-1.14	0.435
High RH	98.72 (254)	100.34 (249)	103.27 (245)	107.34 (254)	8.62	0.64	0.277
Low plus High RH	98.51 (502)	100.28 (491)	102.25 (491)	106.24 (502)	7.73	-0.24	0.846

[a] Transformed from natural logarithm scale.

[b] Difference between 1992 and 1982 examination means after transformation to original scale.

[c] Difference between Ranch Hand dioxin category and Comparison category.

[d] P-value is based on analysis of natural logarithm of fasting glucose; results adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, natural logarithm of fasting glucose in 1982, and age in 1992.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.
Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1982, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations.

Fasting Glucose (All Participants—Discrete)

Longitudinal analyses of fasting glucose were conducted among participants who exhibited normal levels of fasting glucose in 1982. All analyses from Models 1, 2, and 3 were nonsignificant, indicating no association between fasting glucose and group, initial dioxin, or categorized dioxin (Table 18-75(a-c): p>0.14 for all analyses).

2-Hour Postprandial Glucose (Nondiabetics—Continuous)

All results from Models 1, 2, and 3 were nonsignificant from the longitudinal analysis of 2-hour postprandial glucose in nondiabetics (Table 18-76(a-c): p>0.21 for all analyses).

2-Hour Postprandial Glucose (Nondiabetics—Discrete)

Among nondiabetic participants with normal levels of 2-hour postprandial glucose in 1982, differences among Ranch Hands and Comparisons overall were found marginally significant from the Model 1 analysis (Table 18-77(a): p=0.081, Adj. RR=1.32). Of Ranch Hands, 13.5 percent exhibited an impaired level of 2-hour postprandial glucose compared to 10.8 percent of Comparisons. Stratified by occupation, the percent impaired in the officer Ranch Hand category was marginally significantly higher than the corresponding Comparison category (p=0.083, Adj. RR=1.59: 13.1% vs. 8.7% respectively). The Model 2 analysis was limited to participants with normal levels of 2-hour postprandial glucose and revealed a nonsignificant association with initial dioxin (Table 18-77(b): p=0.143).

Among nondiabetic participants with normal levels of 2-hour postprandial glucose, the background Ranch Hands versus Comparisons and low Ranch Hands versus Comparisons contrasts were nonsignificant in the Model 3 longitudinal analysis of 2-hour postprandial glucose (Table 18-77(c): p=0.975 and p=0.352 respectively). However, the high Ranch Hands and low plus high Ranch Hands contrasts were significant (Table 18-77(c): p=0.004, Adj. RR=1.97 and p=0.014, Adj. RR=1.60 respectively). The percentages for those having an impaired level of 2-hour postprandial glucose at the 1992 examination with a normal level in 1982 were 18.4 percent for high Ranch Hands, 16.2 percent for low plus high Ranch Hands, and 10.8 percent for Comparisons (Table 18-77(c)).

Total Testosterone (Continuous)

The Model 1 longitudinal analysis of total testosterone revealed that differences of examination mean change between Ranch Hands and Comparisons were nonsignificant over all and within each occupational strata (Table 18-78(a): p≥0.17 for each contrast). The Model 2 results also were nonsignificant (Table 18-78(b): p=0.721).

The Model 3 analysis of total testosterone displayed a marginally significant difference in examination mean changes between background Ranch Hands and Comparisons (Table 18-78(c): p=0.066, Diff. of Exam. Mean Change=12.30). The change in total testosterone means from 1982 to 1992 for Comparisons was greater than the change for background Ranch Hands. All other Model 3 analyses were nonsignificant (Table 18-78(c): p>0.48 for remaining analyses).

Table 18-75.
Longitudinal Analysis of Fasting Glucose (All Participants)
(Discrete)

a) MODEL 1: RANCH HANDS VS. COMPARISONS					
		Percent Abnormal High/(n) Examination			
Occupational Category	Group	1982	1985	1987	1992
All	*Ranch Hand*	*4.3 (899)*	*9.4 (877)*	*12.3 (867)*	*13.6 (899)*
	Comparison	*3.7 (1,060)*	*9.7 (1,037)*	*13.3 (1,033)*	*13.7 (1,060)*
Officer	Ranch Hand	3.9 (338)	9.6 (333)	13.9 (331)	13.3 (338)
	Comparison	3.2 (403)	8.6 (395)	13.3 (391)	13.4 (403)
Enlisted Flyer	Ranch Hand	7.6 (159)	10.2 (157)	13.0 (154)	13.8 (159)
	Comparison	4.6 (175)	12.2 (172)	16.1 (174)	14.9 (175)
Enlisted Groundcrew	Ranch Hand	3.5 (402)	8.8 (387)	10.7 (382)	13.7 (402)
	Comparison	3.7 (482)	9.8 (470)	12.2 (468)	13.5 (482)

		Normal in 1982			
Occupational Category	Group	n in 1992	Percent Abnormal High in 1992	Adj. Relative Risk (95% C.I.)[a]	p-Value[a]
All	*Ranch Hand*	*860*	*10.4*	*0.94 (0.70,1.27)*	*0.707*
	Comparison	*1,021*	*11.1*		
Officer	Ranch Hand	325	10.2	0.95 (0.58,1.55)	0.835
	Comparison	390	10.8		
Enlisted Flyer	Ranch Hand	147	7.5	0.56 (0.26,1.22)	0.143
	Comparison	167	12.6		
Enlisted Groundcrew	Ranch Hand	388	11.6	1.15 (0.74,1.78)	0.540
	Comparison	464	10.8		

[a] Relative risk, confidence interval, and p-values are in reference to a contrast of 1982 and 1992 results; results adjusted for age in 1992.

Note: Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations. Statistical analyses are based only on participants who had a normal fasting glucose level in 1982 (see Chapter 7, Statistical Methods).

Table 18-75. (Continued)
Longitudinal Analysis of Fasting Glucose (All Participants)
(Discrete)

b) MODEL 2: RANCH HANDS — INITIAL DIOXIN				
	Percent Abnormal High/(n) Examination			
Initial Dioxin	1982	1985	1987	1992
Low	5.4 (166)	10.4 (163)	14.6 (165)	16.9 (166)
Medium	6.6 (168)	13.6 (162)	11.6 (164)	15.5 (168)
High	6.6 (168)	13.3 (166)	19.1 (162)	17.3 (168)

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
	Normal in 1982			
Initial Dioxin	n in 1992	Percent Abnormal High in 1992	Adj. Relative Risk (95% C.I.)[b]	p-Value
Low	157	12.1	1.11 (0.89,1.40)	0.356
Medium	157	10.8		
High	157	12.1		

[a] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to date of blood draw for dioxin, and age in 1992.

[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.
Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations. Statistical analyses are based only on participants who had a normal fasting glucose level in 1982 (see Chapter 7, Statistical Methods).

Table 18-75. (Continued)
Longitudinal Analysis of Fasting Glucose (All Participants)
(Discrete)

c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY

	Percent Abnormal High/(n) Examination			
Dioxin Category	1982	1985	1987	1992
Comparison	3.4 (914)	9.2 (903)	13.2 (904)	13.6 (914)
Background RH	2.3 (342)	6.2 (339)	9.0 (335)	9.7 (342)
Low RH	6.1 (248)	12.0 (242)	14.2 (246)	17.3 (248)
High RH	6.3 (254)	12.9 (249)	15.9 (245)	15.8 (254)
Low plus High RH	6.2 (502)	12.4 (491)	15.1 (491)	16.5 (502)

	Normal in 1982			
Dioxin Category	n in 1992	Percent Abnormal High in 1992	Adj. Relative Risk (95% C.I.)[ab]	p-Value[b]
Comparison	883	11.3		
Background RH	334	8.4	0.81 (0.51,1.28)	0.360
Low RH	233	12.5	0.90 (0.56,1.44)	0.651
High RH	238	10.9	0.96 (0.59,1.57)	0.871
Low plus High RH	471	11.7	0.93 (0.64,1.35)	0.686

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to date of blood draw for dioxin, and age in 1992.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤10 ppt.
Background (Ranch Hand): Current Dioxin ≤10 ppt.
Low (Ranch Hand): Current Dioxin >10 ppt, 10 ppt < Initial Dioxin ≤143 ppt.
High (Ranch Hand): Current Dioxin >10 ppt, Initial Dioxin > 143 ppt.
Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations. Statistical analyses are based only on participants who had a normal fasting glucose level in 1982 (see Chapter 7, Statistical Methods).

Table 18-76.
Longitudinal Analysis of 2-Hour Postprandial Glucose (mg/dl) (Nondiabetics)
(Continuous)

a) MODEL 1: RANCH HANDS VS. COMPARISONS								
		Mean[a]/(n) Examination						
Occupational Category	Group	1982	1985	1987	1992	Exam. Mean Change[b]	Difference of Exam. Mean Change	p-Value[c]
All	*Ranch Hand*	*90.52 (758)*	*102.16 (736)*	*106.83 (724)*	*104.03 (758)*	*13.51*	*-0.95*	*0.504*
	Comparison	*90.69 (902)*	*104.32 (875)*	*106.42 (867)*	*105.15 (902)*	*14.46*		
Officer	Ranch Hand	90.00 (285)	104.75 (279)	107.61 (279)	104.12 (285)	14.12	0.60	0.745
	Comparison	89.83 (354)	103.22 (344)	105.91 (341)	103.35 (354)	13.51		
Enlisted Flyer	Ranch Hand	91.87 (134)	101.09 (132)	108.75 (129)	105.70 (134)	13.82	-0.57	0.596
	Comparison	94.62 (144)	108.64 (141)	109.35 (141)	109.01 (144)	14.39		
Enlisted Groundcrew	Ranch Hand	90.43 (339)	100.42 (325)	105.38 (316)	103.31 (339)	12.88	-2.43	0.330
	Comparison	90.08 (404)	103.77 (390)	105.82 (385)	105.40 (404)	15.31		

[a] Transformed from natural logarithm scale.

[b] Difference between 1992 and 1982 examination means after transformation to original scale.

[c] P-value is based on analysis of natural logarithm of 2-hour postprandial glucose; results adjusted for natural logarithm of 2-hour postprandial glucose in 1982 and age in 1992.

Note: Summary statistics for 1982 and 1992 are provided for participants who attended the Baseline and 1992 examinations and were nondiabetic in 1982 and 1992. Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations and were nondiabetic in 1985. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations and were nondiabetic in 1987.

Table 18-76. (Continued)
Longitudinal Analysis of 2-Hour Postprandial Glucose (mg/dl) (Nondiabetics) (Continuous)

b) MODEL 2: RANCH HANDS — INITIAL DIOXIN						
	Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]	
	Mean[a]/(n) Examination					
Initial Dioxin	1982	1985	1987	1992	Adj. Slope (Std. Error)	p-Value
Low	91.68 (135)	103.29 (131)	109.23 (133)	103.47 (135)	0.013 (0.011)	0.211
Medium	92.14 (137)	104.74 (131)	106.22 (132)	107.11 (137)		
High	92.43 (134)	101.97 (132)	109.36 (126)	108.05 (134)		

[a] Transformed from natural logarithm scale.

[b] Results based on difference between natural logarithm of 2-hour postprandial glucose in 1992 and natural logarithm of 2-hour postprandial glucose in 1982 versus $\log_2$ (initial dioxin); results adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to date of blood draw for dioxin, natural logarithm of 1982 2-hour postprandial glucose, and age in 1992.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.
Summary statistics for 1982 and 1992 are provided for participants who attended the Baseline and 1992 examinations and were nondiabetic in 1982 and 1992. Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations and were nondiabetic in 1985. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations and were nondiabetic in 1987.

Table 18-76. (Continued)
Longitudinal Analysis of 2-Hour Postprandial Glucose (mg/dl) (Nondiabetics) (Continuous)

c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY							
	Mean[a]/(n) Examination						
Dioxin Category	1982	1985	1987	1992	Exam. Mean Change[b]	Difference of Exam. Mean Change[c]	p-Value[d]
Comparison	90.81 (778)	104.25 (764)	106.81 (761)	104.79 (778)	13.98		
Background RH	88.47 (301)	101.20 (297)	105.64 (295)	100.93 (301)	12.45	-1.53	0.333
Low RH	92.50 (199)	103.93 (191)	108.86 (195)	104.96 (199)	12.47	-1.52	0.499
High RH	91.69 (207)	102.76 (203)	107.64 (196)	107.39 (207)	15.70	1.71	0.220
Low plus High RH	92.08 (406)	103.32 (394)	108.25 (391)	106.19 (406)	14.11	0.12	0.721

[a] Transformed from natural logarithm scale.

[b] Difference between 1992 and 1982 examination means after transformation to original scale.

[c] Difference between Ranch Hand dioxin category and Comparison dioxin category.

[d] P-value is based on analysis of natural logarithm of 2-hour postprandial glucose; results adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, natural logarithm of 2-hour postprandial glucose in 1982, and age in 1992.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤10 ppt.
Background (Ranch Hand): Current Dioxin ≤10 ppt.
Low (Ranch Hand): Current Dioxin >10 ppt, 10 ppt < Initial Dioxin ≤143 ppt.
High (Ranch Hand): Current Dioxin >10 ppt, Initial Dioxin >143 ppt.
Summary statistics for 1982 and 1992 are provided for participants who attended the Baseline and 1992 examinations and were nondiabetic in 1982 and 1992. Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations and were nondiabetic in 1985. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations and were nondiabetic in 1987.

Table 18-77.
Longitudinal Analysis of 2-Hour Postprandial Glucose (Nondiabetics) (Discrete)

a) MODEL 1: RANCH HANDS VS. COMPARISONS

Occupational Category	Group	Percent Impaired/(n) Examination 1982	1985	1987	1992
All	***Ranch Hand***	***6.5 (758)***	***8.6 (736)***	***13.7 (724)***	***15.2 (758)***
	Comparison	***6.9 (902)***	***11.1 (875)***	***10.8 (867)***	***13.1 (902)***
Officer	Ranch Hand	6.0 (285)	9.3 (279)	12.5 (279)	13.7 (285)
	Comparison	6.2 (354)	9.3 (344)	9.1 (341)	11.6 (354)
Enlisted Flyer	Ranch Hand	6.7 (134)	9.1 (132)	18.6 (129)	14.2 (134)
	Comparison	13.2 (144)	16.3 (141)	15.6 (141)	16.7 (144)
Enlisted Groundcrew	Ranch Hand	6.8 (339)	7.7 (325)	12.7 (316)	16.8 (339)
	Comparison	5.2 (404)	10.8 (390)	10.7 (385)	13.1 (404)

Occupational Category	Group	Normal in 1982: n in 1992	Normal in 1982: Percent Impaired in 1992	Adj. Relative Risk (95% C.I.)[a]	p-Value[a]
All	***Ranch Hand***	***709***	***13.5***	***1.32 (0.97,1.79)***	***0.081***
	Comparison	***840***	***10.8***		
Officer	Ranch Hand	268	13.1	1.59 (0.94,2.69)	0.083
	Comparison	332	8.7		
Enlisted Flyer	Ranch Hand	125	12.0	0.87 (0.41,1.84)	0.722
	Comparison	125	13.6		
Enlisted Groundcrew	Ranch Hand	316	14.6	1.36 (0.87,2.13)	0.176
	Comparison	383	11.8		

[a] Relative risk, confidence interval, and p-values are in reference to a contrast of 1982 and 1992 results; results adjusted for age in 1992.

Note: Summary statistics for 1982 and 1992 are provided for participants who attended the Baseline and 1992 examinations and were nondiabetic in 1982 and 1992. Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations and were nondiabetic in 1985. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations and were nondiabetic in 1987. Statistical analyses are based only on participants who had a normal 2-hour postprandial glucose level in 1982 (see Chapter 7, Statistical Methods).

Table 18-77. (Continued)
Longitudinal Analysis of 2-Hour Postprandial Glucose (Nondiabetics) (Discrete)

b) MODEL 2: RANCH HANDS — INITIAL DIOXIN				
	Percent Impaired/(n) Examination			
Initial Dioxin	1982	1985	1987	1992
Low	7.4 (135)	9.9 (131)	14.3 (133)	16.3 (135)
Medium	8.8 (137)	8.4 (131)	12.9 (132)	17.5 (137)
High	6.0 (134)	10.6 (132)	16.7 (126)	20.9 (134)

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
	Normal in 1982			
Initial Dioxin	n in 1992	Percent Impaired in 1992	Adj. Relative Risk (95% C.I.)[b]	p-Value
Low	125	13.6	1.18 (0.95,1.49)	0.143
Medium	125	16.0		
High	126	19.1		

[a] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to date of blood draw for dioxin, and age in 1992.

[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.
Summary statistics for 1982 and 1992 are provided for participants who attended the Baseline and 1992 examinations and were nondiabetic in 1982 and 1992. Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations and were nondiabetic in 1985. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations and were nondiabetic in 1987. Statistical analyses are based only on participants who had a normal 2-hour postprandial glucose level in 1982 (see Chapter 7, Statistical Methods).

Table 18-77. (Continued)
Longitudinal Analysis of 2-Hour Postprandial Glucose (Nondiabetics)
(Discrete)

c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY

	Percent Impaired/(n) Examination			
Dioxin Category	**1982**	**1985**	**1987**	**1992**
Comparison	6.9 (778)	10.7 (764)	10.5 (761)	12.7 (778)
Background RH	5.3 (301)	6.4 (297)	12.9 (295)	10.6 (301)
Low RH	9.6 (199)	10.5 (191)	14.4 (195)	16.6 (199)
High RH	5.3 (207)	8.9 (203)	14.8 (196)	19.8 (207)
Low plus High RH	7.4 (406)	9.6 (394)	14.6 (391)	18.2 (406)

	Normal in 1982			
Dioxin Category	**n in 1992**	**Percent Impaired in 1992**	**Adj. Relative Risk (95% C.I.)[ab]**	**p-Value[b]**
Comparison	724	10.8		
Background RH	285	9.8	0.99 (0.62,1.59)	0.975
Low RH	180	13.9	1.27 (0.77,2.10)	0.352
High RH	196	18.4	1.97 (1.25,3.11)	0.004
Low plus High RH	376	16.2	1.60 (1.10,2.34)	0.014

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to date of blood draw for dioxin, and age in 1992.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤10 ppt.
Background (Ranch Hand): Current Dioxin ≤10 ppt.
Low (Ranch Hand): Current Dioxin >10 ppt, 10 ppt < Initial Dioxin ≤143 ppt.
High (Ranch Hand): Current Dioxin >10 ppt, Initial Dioxin > 143 ppt.
Summary statistics for 1982 and 1992 are provided for participants who attended the Baseline and 1992 examinations and were nondiabetic in 1982 and 1992. Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations and were nondiabetic in 1985. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations and were nondiabetic in 1987. Statistical analyses are based only on participants who had a normal 2-hour postprandial glucose level in 1982 (see Chapter 7, Statistical Methods).

Table 18-78.
Longitudinal Analysis of Total Testosterone (ng/dl)
(Continuous)

a) MODEL 1: RANCH HANDS VS. COMPARISONS								
		Mean[a]/(n) Examination						
Occupational Category	Group	1982	1985	1987	1992	Exam. Mean Change[b]	Difference of Exam. Mean Change	p-Value[c]
All	*Ranch Hand*	*638.00 (886)*	*598.27 (861)*	*530.88 (854)*	*511.29 (886)*	*-126.70*	*-1.80*	*0.488*
	Comparison	*623.23 (1,054)*	*575.38 (1,030)*	*523.57 (1,028)*	*498.33 (1,054)*	*-124.90*		
Officer	Ranch Hand	603.45 (331)	570.15 (323)	506.00 (324)	494.76 (331)	-108.70	14.96	0.170
	Comparison	601.18 (401)	554.17 (394)	498.79 (390)	477.53 (401)	-123.65		
Enlisted Flyer	Ranch Hand	648.81 (158)	614.90 (156)	526.70 (153)	528.21 (158)	-120.60	9.77	0.280
	Comparison	628.51 (173)	568.55 (169)	529.38 (172)	498.15 (173)	-130.37		
Enlisted Groundcrew	Ranch Hand	663.15 (397)	615.71 (382)	554.47 (377)	518.54 (397)	-144.61	-20.69	0.371
	Comparison	640.04 (480)	596.11 (467)	542.60 (466)	516.12 (480)	-123.92		

[a] Transformed from square root scale.

[b] Difference between 1992 and 1982 examination means after transformation to original scale.

[c] P-value is based on analysis of square root of total testosterone; results adjusted for square root of total testosterone in 1982; and age in 1992.

Note: Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations.

Table 18-78. (Continued)
Longitudinal Analysis of Total Testosterone (ng/dl)
(Continuous)

b) MODEL 2: RANCH HANDS — INITIAL DIOXIN						
	Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]	
	Mean[a]/(n) Examination					
Initial Dioxin	1982	1985	1987	1992	Adj. Slope (Std. Error)	p-Value
Low	633.88 (165)	559.58 (161)	521.46 (164)	508.79 (165)	0.045 (0.127)	0.721
Medium	620.68 (166)	565.47 (160)	514.48 (162)	484.20 (166)		
High	609.44 (168)	584.23 (166)	506.01 (162)	478.89 (168)		

[a] Transformed from square root scale.

[b] Results based on difference between square root of total testosterone in 1992 and square root of total testosterone in 1982 versus $\log_2$ (initial dioxin); results adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to date of blood draw for dioxin, square root of 1982 total testosterone, and age in 1992.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.
Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations.

Table 18-78. (Continued)
Longitudinal Analysis of Total Testosterone (ng/dl)
(Continuous)

c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY							
	Mean[a]/(n) Examination						
Dioxin Category	1982	1985	1987	1992	Exam. Mean Change[b]	Difference of Exam. Mean Change[c]	p-Value[d]
Comparison	624.73 (910)	576.62 (897)	522.09 (900)	497.33 (910)	-127.40		
Background RH	657.21 (333)	635.27 (329)	551.02 (326)	542.11 (333)	-115.10	12.30	0.066
Low RH	631.40 (246)	558.05 (239)	516.79 (244)	504.60 (246)	-126.81	0.60	0.581
High RH	611.40 (253)	581.38 (248)	511.21 (244)	476.90 (253)	-134.50	-7.10	0.485
Low plus High RH	621.22 (499)	569.87 (487)	513.99 (488)	490.46 (499)	-130.77	-3.36	0.925

[a] Transformed from square root scale.

[b] Difference between 1992 and 1982 examination means after transformation to original scale.

[c] Difference between Ranch Hand dioxin category and Comparison dioxin category.

[d] P-value is based on analysis of square root of total testosterone; results adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, square root of total testosterone in 1982, and age in 1992.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤10 ppt.
Background (Ranch Hand): Current Dioxin ≤10 ppt.
Low (Ranch Hand): Current Dioxin >10 ppt, 10 ppt < Initial Dioxin ≤143 ppt.
High (Ranch Hand): Current Dioxin >10 ppt, Initial Dioxin >143 ppt.
Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations.

Total Testosterone (Discrete)

Longitudinal analyses of total testosterone were conducted among participants who exhibited normal levels of total testosterone in 1982. All analyses from Models 1, 2, and 3 were each nonsignificant indicating no association between total testosterone and group, initial dioxin, or categorized dioxin (Table 18-79(a-c): $p>0.14$ for all analyses).

DISCUSSION

The historical, physical examination, and laboratory data analyzed in this chapter provide a comprehensive assessment of thyroid, gonadal, and endocrine pancreatic function in the population under study. The current laboratory database was expanded to include several indices relevant to the possibility that dioxin may influence glucose metabolism. Alpha-1-C hemoglobin reflects the average blood sugar over a 3-4 month period and is a more accurate index of diabetic control than random or fasting blood sugar measurements. All participants with diabetes were of the adult-onset (Type II) variety, usually secondary to obesity and characterized by an acquired defect in insulin receptors with elevated serum insulin levels. In the production of insulin by the pancreatic islet beta cell, proinsulin is cleaved to form insulin and c-peptide (connecting-peptide). C-peptide is considered a marker for endogenous secretion of insulin. Proinsulin in serum consists of insulin plus c-peptide that was not cleaved during secretion and is an index of beta cell secretory activity. Additional physical examination variables pertinent to endocrine function—body habitus, ocular signs, and deep tendon reflexes—were included in the general and neurological examinations and are reported in Chapters 9 and 11 respectively. Integumentary manifestations of diabetes (cutaneous infections, signs of arterial occlusive or venous stasis, and onychomycosis) and thyroid disorders (e.g., pigmentary and nail changes and thinning of hair) are described in Chapter 14, Dermatology Assessment.

Measures of LH, FSH, estradiol, and testosterone are used to detect and determine the location of hormone defects in the hypothalamus, pituitary, or gonads. Elevations in any of these indices typically reflect primary failure of one of these three organs. In men, such disorders may be manifested clinically as hypogonadism, sexual dysfunction, or gynecomastia. Possible etiologies include toxic exposure, neoplasms, infections, or surgical intervention (e.g., orchiectomy for testicular cancer).

In the analysis of historical variables verified by medical record review, the prevalence of thyroid disorders and diabetes mellitus was similar in the Ranch Hand and Comparison cohorts (5.3% versus 5.6% and 15.0% versus 14.0% respectively). Among Ranch Hands, in a pattern consistent with a dose-response, a significant positive association was noted between the current body burden of dioxin and the development of diabetes, specifically in the early stages requiring only dietary intervention or oral hypoglycemic therapy. Ranch Hands with higher levels of current serum dioxin were significantly more likely to develop diabetes sooner after their exposure than those with lower serum dioxin levels.

In the evaluation of thyroid functions by serum T_4 and TSH, no significant group differences were defined. Consistent with the 1985 and 1987 examinations, Ranch Hands continued to have a slightly higher mean serum TSH than Comparisons (1.62 mIU/ml versus

Table 18-79.
Longitudinal Analysis of Total Testosterone
(Discrete)

a) MODEL 1: RANCH HANDS VS. COMPARISONS

Occupational Category	Group	Percent Abnormal Low/(n) Examination 1982	1985	1987	1992
All	***Ranch Hand***	***4.6 (886)***	***2.9 (861)***	***1.9 (854)***	***4.5 (886)***
	Comparison	***4.9 (1,054)***	***3.0 (1,030)***	***1.5 (1,028)***	***5.6 (1,054)***
Officer	Ranch Hand	4.5 (331)	3.7 (323)	1.9 (324)	4.8 (331)
	Comparison	5.0 (401)	3.8 (394)	2.1 (390)	5.0 (401)
Enlisted Flyer	Ranch Hand	6.3 (158)	2.6 (156)	3.3 (153)	3.8 (158)
	Comparison	5.8 (173)	4.1 (169)	0.6 (172)	5.8 (173)
Enlisted Groundcrew	Ranch Hand	4.0 (397)	2.4 (382)	1.3 (377)	4.5 (397)
	Comparison	4.6 (480)	1.9 (467)	1.3 (466)	6.0 (480)

Occupational Category	Group	Normal in 1982: n in 1992	Normal in 1982: Percent Abnormal Low in 1992	Adj. Relative Risk (95% C.I.)[a]	p-Value[a]
All	***Ranch Hand***	***845***	***3.6***	***0.84 (0.52,1.36)***	***0.486***
	Comparison	***1,002***	***4.2***		
Officer	Ranch Hand	316	4.1	1.21 (0.55,2.66)	0.627
	Comparison	381	3.4		
Enlisted Flyer	Ranch Hand	148	2.7	0.62 (0.18,2.16)	0.453
	Comparison	163	4.3		
Enlisted Groundcrew	Ranch Hand	381	3.4	0.71 (0.35,1.43)	0.337
	Comparison	458	4.8		

[a] Relative risk, confidence interval, and p-values are in reference to a contrast of 1982 and 1992 results; results adjusted for age in 1992.

Note: Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations. Statistical analyses are based only on participants who had a normal total testosterone level in 1982 (see Chapter 7, Statistical Methods).

Table 18-79. (Continued)
Longitudinal Analysis of Total Testosterone
(Discrete)

b) MODEL 2: RANCH HANDS — INITIAL DIOXIN				
	Percent Abnormal Low/(n) Examination			
Initial Dioxin	1982	1985	1987	1992
Low	4.2 (165)	2.5 (161)	3.7 (164)	4.2 (165)
Medium	5.4 (166)	3.1 (160)	1.2 (162)	4.8 (166)
High	7.1 (168)	2.4 (166)	2.5 (162)	8.3 (168)

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
	Normal in 1982			
Initial Dioxin	n in 1992	Percent Abnormal Low in 1992	Adj. Relative Risk (95% C.I.)[b]	p-Value
Low	158	2.5	1.20 (0.88,1.65)	0.254
Medium	157	4.5		
High	156	7.1		

[a] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to date of blood draw for dioxin, and age in 1992.

[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.
Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations. Statistical analyses are based only on participants who had a normal total testosterone level in 1982 (see Chapter 7, Statistical Methods).

Table 18-79. (Continued)
Longitudinal Analysis of Total Testosterone (Discrete)

c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY

	Percent Abnormal Low/(n) Examination			
Dioxin Category	**1982**	**1985**	**1987**	**1992**
Comparison	5.0 (910)	2.9 (897)	1.4 (900)	5.5 (910)
Background RH	3.3 (333)	3.0 (329)	0.9 (326)	2.4 (333)
Low RH	4.9 (246)	2.1 (239)	3.3 (244)	4.1 (246)
High RH	6.3 (253)	3.2 (248)	1.64 (244)	7.5 (253)
Low plus High RH	5.6 (499)	2.7 (487)	2.5 (488)	5.8 (499)

	Normal in 1982			
Dioxin Category	**n in 1992**	**Percent Abnormal Low in 1992**	**Adj. Relative Risk (95% C.I.)[ab]**	**p-Value[b]**
Comparison	865	3.8		
Background RH	322	2.2	0.76 (0.33,1.76)	0.515
Low RH	234	3.0	0.68 (0.29,1.57)	0.363
High RH	237	6.3	1.63 (0.85,3.12)	0.143
Low plus High RH	471	4.7	1.12 (0.64,1.98)	0.685

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to date of blood draw for dioxin, and age in 1992.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤10 ppt.
Background (Ranch Hand): Current Dioxin ≤10 ppt.
Low (Ranch Hand): Current Dioxin >10 ppt, 10 ppt < Initial Dioxin ≤143 ppt.
High (Ranch Hand): Current Dioxin >10 ppt, Initial Dioxin > 143 ppt.
Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations. Statistical analyses are based only on participants who had a normal total testosterone level in 1982 (see Chapter 7, Statistical Methods).

1.57 mIU/ml), but the difference is no longer statistically significant. In addition, by discrete analysis, the prevalence of abnormal TSH and T_4 results was virtually identical in the two cohorts.

With reference to the laboratory assessment of glucose metabolism and, particularly, the possibility that dioxin might be a risk factor for the development of diabetes, significant results were, for the most part, limited to the analyses employing current serum dioxin. In contrast to the Baseline examination results, in which glucose intolerance was more prevalent in Comparisons than in Ranch Hands, none of the laboratory variables from the 1992 examination, in both continuous and discrete analyses, revealed any significant group differences.

In the continuous analysis of all Ranch Hand participants, those with high levels of serum dioxin had significantly higher fasting glucose and 2-hour postprandial glucose results than those with lower levels of serum dioxin. Stratification of the Ranch Hand cohort by disease status revealed that the fasting glucose results were driven primarily by the diabetic subset. In contrast, in nondiabetics, a slight negative association was noted: those with lower levels of serum dioxin were more likely to have elevated fasting glucose than those with higher serum dioxin levels.

The analyses of serum insulin levels raise additional questions and point to a potential mechanism for an effect of dioxin on glucose metabolism. In the natural history of adult-onset diabetes mellitus, serum insulin levels vary depending on the stage of the disease. Initially, as glucose intolerance develops, serum insulin levels typically rise. In nondiabetic Ranch Hands, serum insulin, like the 2-hour postprandial glucose, was positively and significantly associated with current serum dioxin, an effect that was pronounced in both the high and low levels of exposure in the discrete analysis. In contrast, in diabetic participants, a consistent inverse dose-response was found in all models relating serum insulin to current serum dioxin. Although not statistically significant, these data are consistent with a fundamental impairment of islet cell responsiveness to hyperglycemia with increased insulin production in nondiabetics and, in diabetes, an impaired compensatory response with compromised insulin production.

The analysis of serum C peptide and serum proinsulin and α-1-c hemoglobin yielded no significant results and failed to shed light on the biochemical mechanisms, if any, by which dioxin might have an effect on insulin production and glucose metabolism.

With respect to gonadal function, no significant group differences were defined. Testicular volume, assessed more accurately in these examinations by ultrasound rather than by palpitation, was virtually identical in Ranch Hands and Comparisons. As in the Baseline and 1985 examinations, Ranch Hands had a higher mean total testosterone level than Comparisons, but the difference was no longer significant. These results are in contrast to those documented in experimental studies on animals discussed in the background section of this chapter.

The analysis of total serum testosterone yielded results consistent with a dioxin effect. Ranch Hands with high current serum dioxin had significantly lower total testosterone levels

than those with lower current serum dioxin levels. In the continuous analysis of the biologically active free form of testosterone, however, there was no evidence of a dose-response effect. Though these results are consistent with those documented in the Serum Dioxin Analysis of the 1987 Followup Examination, the clinical significance remains uncertain.

Dependent variable-covariate analyses confirmed associations that are well established in clinical practice. The classic risk factors of age, obesity, and family history of diabetes were strongly and positively associated with all diabetic indices. A significant negative association was noted between age and testicular size and serum testosterone. Age, diabetes, family history of diabetes, and, particularly, cigarette use all contributed strongly to the development of pulse deficits and arterial occlusive disease.

The longitudinal analyses yielded results that would be anticipated over time with no significant differences between Ranch Hands and Comparisons. Age-related increases were documented in fasting glucose, 2-hour postprandial glucose, and the incidence of diabetes. Serum testosterone decreased with advancing years.

In summary, after 10 years of observation, the prevalence of endocrine disease remains similar in Ranch Hands and Comparisons. Though cause and effect remain to be established, the data cited above provide further evidence for an association between glucose intolerance and dioxin exposure. Also raised is the possibility that, in a subset of individuals predisposed to diabetes, dioxin may impair insulin production.

SUMMARY

Analyses were performed on 36 dependent variables derived from medical records, physical examination, and laboratory procedures for the endocrine assessment. Fourteen variables were analyzed both continuously and discretely, and separate analyses for all participants, diabetics, and nondiabetics were executed for five endpoints. Each of these variables was investigated for possible associations with group (Model 1), initial or categorized dioxin (Models 2 and 3), and current dioxin (Models 4, 5, and 6). Summarized results from these analyses are shown in Table 18-80 through 18-83. A list of group-by-covariate and dioxin-by-covariate interactions that were significant in the Model 1 through 6 adjusted analyses is presented in Table 18-84.

Model 1: Group Analysis

Only one association of marginal significance between group and the thyroid endpoints was found in the unadjusted and adjusted analyses for Model 1. Overall, abnormality percentages for anti-thyroid antibodies were greater in the Ranch Hand category than in the Comparison category, but occupationally-stratified contrasts were nonsignificant.

In the analyses of the diabetes variables, several endpoints exhibited significant interactions primarily with age, body fat, or both, but results were nonsignificant when these interaction terms were deleted from the final model. A single exception to this finding was in the analysis of fasting glucose, where after deleting the interaction term, nondiabetic enlisted

Table 18-80.
Summary of Group Analyses (Model 1) for Endocrine Variables (Ranch Hands vs. Comparisons)

Variable	UNADJUSTED			
	All	Officer	Enlisted Flyer	Enlisted Groundcrew
Verified Medical Records				
Past Thyroid Disease (D)	ns	NS	NS	ns
Composite Diabetes Indicator (D)	NS	NS	ns	ns
Diabetic Severity (D)				
No Treatment vs. Nondiabetic	ns	NS	ns	ns
Diet Only vs. Nondiabetic	NS	NS*	ns	NS
Oral Hypoglycemic vs. Nondiabetic	ns	ns	NS	NS
Insulin Dependent vs. Nondiabetic	NS*	NS*	NS	NS
Time to Diabetes Onset[a] (C)	ns	NS	ns	ns
Physical Examination				
Thyroid Gland (D)	ns	ns	--	ns
Testicular Volume: Minimum[a] (C)	NS	NS	ns	NS
Testicular Volume: Total[a] (C)	ns	ns	ns	NS
Retinopathy Results (Diabetics) (D)	NS	NS	--	ns
Neuropathy Results (Diabetics) (D)	NS	NS	ns	NS*
Radial Pulses (Doppler) (Diabetics) (D)	NS	NS	--	--
Femoral Pulses (Doppler) (Diabetics) (D)	NS	--	ns	ns
Popliteal Pulses (Doppler) (Diabetics) (D)	NS	--	ns	NS
Dorsalis Pedis Pulses (Doppler) (Diabetics) (D)	NS	NS	ns	NS
Posterior Tibial Pulses (Doppler) (Diabetics) (D)	NS	NS	ns	NS
Leg Pulses (Doppler) (Diabetics) (D)	NS	NS	ns	NS
Peripheral Pulses (Doppler) (Diabetics) (D)	NS	NS	ns	NS
Laboratory				
Thyroid Stimulating Hormone (TSH) (C)	NS	NS	ns	NS
Thyroid Stimulating Hormone (TSH) (D)	NS	ns	NS	NS
Thyroxine (T_4)[a] (C)	ns	ns	NS	ns
Thyroxine (T_4) (D)	NS	NS	--	--
Anti-Thyroid Antibodies (D)	NS*	NS	NS	NS
Fasting Glucose (All Participants) (C)	ns	NS	ns	NS
Fasting Glucose (All Participants) (D)	NS	NS	ns	NS
Fasting Glucose (Diabetics) (C)	ns	ns	ns	ns

Table 18-80. (Continued)
Summary of Group Analyses (Model 1) for Endocrine Variables
(Ranch Hands vs. Comparisons)

	UNADJUSTED			
Variable	**All**	**Officer**	**Enlisted Flyer**	**Enlisted Groundcrew**
Fasting Glucose (Diabetics) (D)	ns	ns	NS	ns
Fasting Glucose (Nondiabetics) (C)	ns	NS	-0.015	NS
Fasting Glucose (Nondiabetics) (D)	ns	ns	ns	NS
2-Hour Postprandial Glucose (Nondiabetics) (C)	NS	NS	ns	ns
2-Hour Postprandial Glucose (Nondiabetics) (D)	NS*	NS	ns	NS
Fasting Urinary Glucose (All Participants) (D)	NS	ns	ns	NS
Fasting Urinary Glucose (Diabetics) (D)	ns	ns	ns	NS
Fasting Urinary Glucose (Nondiabetics) (D)	--	--	--	--
2-Hour Postprandial Urinary Glucose (Nondiabetics) (D)	NS	NS	ns	NS
Serum Insulin (All Participants) (C)	NS	NS*	ns	ns
Serum Insulin (All Participants) (D)				
Low vs. Normal	ns	ns	NS	NS
High vs. Normal	ns	NS	ns	ns
Serum Insulin (Diabetics) (C)	NS	NS	NS	NS
Serum Insulin (Diabetics) (D)	NS	NS	ns	ns
Serum Insulin (Nondiabetics) (C)	ns	NS	ns	ns
Serum Insulin (Nondiabetics) (D)				
Low vs. Normal	ns	ns	NS	NS
High vs. Normal	ns	ns	ns	ns
Serum Glucagon (All Participants) (C)	ns	ns	-0.031	NS
Serum Glucagon (All Participants) (D)	NS	--	--	NS
Serum Glucagon (Diabetics) (C)	NS	NS	ns	NS
Serum Glucagon (Diabetics) (D)	NS	--	--	NS
Serum Glucagon (Nondiabetics) (C)	ns	ns	ns*	ns
Serum Glucagon (Nondiabetics) (D)	--	--	--	--
α-1-C Hemoglobin (All Participants) (C)	NS	NS	ns	NS
α-1-C Hemoglobin (All Participants) (D)	NS	NS	ns	NS
α-1-C Hemoglobin (Diabetics) (C)	NS	ns	ns	NS
α-1-C Hemoglobin (Diabetics) (D)	NS	NS	ns	NS
α-1-C Hemoglobin (Nondiabetics) (C)	ns	ns	ns	NS
α-1-C Hemoglobin (Nondiabetics) (D)	ns	ns	ns	NS

Table 18-80. (Continued)
Summary of Group Analyses (Model 1) for Endocrine Variables
(Ranch Hands vs. Comparisons)

Variable	UNADJUSTED			
	All	Officer	Enlisted Flyer	Enlisted Groundcrew
Urinary Protein (Diabetics) (D)	ns	NS	NS	ns
Serum Proinsulin (Diabetics) (C)	ns	ns	NS	NS
Serum Proinsulin (Diabetics) (D)	ns	ns	ns	NS
Serum C Peptide (Diabetics) (C)	NS	NS	NS	NS
Serum C Peptide (Diabetics) (D)	NS	ns	NS	ns
Total Testosterone (C)[a]	NS	NS	NS*	NS
Total Testosterone (D)	ns	NS	ns	ns
Free Testosterone (C)[a]	NS	NS	NS	NS
Free Testosterone (D)	-0.014	ns	-0.012	ns
Sex Hormone Binding Globulin (D)	ns*	ns	ns	ns*
Total Testosterone to Sex Hormone Binding Globulin Ratio (D)	ns	ns	ns	NS
Estradiol (C)	ns	ns	NS	ns
Estradiol (D)	ns	ns	NS	NS
Luteinizing Hormone (LH) (C)	NS	NS	NS	NS
Luteinizing Hormone (LH) (D)	ns	ns	NS	NS
Follicle Stimulating Hormone (FSH) (C)	NS	NS	NS	ns
Follicle Stimulating Hormone (FSH) (D)	NS	NS*	NS	ns

[a] Negative difference considered adverse for this variable.
C: Continuous analysis.
D: Discrete analysis.
-: Relative risk < 1.00 for discrete analysis or difference of means negative for continuous analysis.
--: Analysis not performed due to sparse number of abnormalities.
NS or ns: Not significant ($p>0.10$).
NS* or ns*: Marginally significant ($0.05<p\leq0.10$).
Note: P-value given if $p\leq0.05$.
A capital "NS" denotes a relative risk 1.00 or greater for discrete analysis or difference of means nonnegative for continuous analysis; a lower case "ns" denotes relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

Table 18-80. (Continued)
Summary of Group Analyses (Model 1) for Endocrine Variables
(Ranch Hands vs. Comparisons)

	ADJUSTED			
Variable	All	Officer	Enlisted Flyer	Enlisted Groundcrew
Verified Medical Records				
Past Thyroid Disease (D)	**(ns)	**(NS)	**(NS)	**(ns)
Composite Diabetes Indicator (D)	NS	NS	ns	NS
Diabetic Severity (D)				
No Treatment vs. Nondiabetic	ns	NS	ns	ns
Diet Only vs. Nondiabetic	NS	NS	ns	NS
Oral Hypoglycemic vs. Nondiabetic	ns	ns	NS	NS
Insulin Dependent vs. Nondiabetic	NS	NS*	ns	NS
Time to Diabetes Onset[a] (C)	ns	NS	ns	ns
Physical Examination				
Thyroid Gland (D)	ns	ns	--	ns
Testicular Volume: Minimum[a] (C)	NS	NS	ns	NS
Testicular Volume: Total[a] (C)	ns	ns	ns	NS
Retinopathy Results (Diabetics) (D)	**(NS)	**(ns)	--	**(ns)
Neuropathy Results (Diabetics) (D)	NS	NS	ns	NS*
Radial Pulses (Doppler) (Diabetics) (D)	--	--	--	--
Femoral Pulses (Doppler) (Diabetics) (D)	NS	--	ns	ns
Popliteal Pulses (Doppler) (Diabetics) (D)	NS	--	ns	NS
Dorsalis Pedis Pulses (Doppler) (Diabetics) (D)	NS	NS	ns	NS
Posterior Tibial Pulses (Doppler) (Diabetics) (D)	NS	NS	ns	NS
Leg Pulses (Doppler) (Diabetics) (D)	NS	NS	ns	NS
Peripheral Pulses (Doppler) (Diabetics) (D)	NS	NS	ns	NS
Laboratory				
Thyroid Stimulating Hormone (TSH) (C)	NS	NS	ns	NS
Thyroid Stimulating Hormone (TSH) (D)	NS	ns	NS	NS
Thyroxine (T_4)[a](C)	ns	ns	NS	ns
Thyroxine (T_4) (D)	NS	NS	--	--
Anti-Thyroid Antibodies (D)	NS*	NS	NS	NS
Fasting Glucose (All Participants) (C)	NS	NS	ns	NS
Fasting Glucose (All Participants) (D)	NS	NS	ns	NS
Fasting Glucose (Diabetics) (C)	**(ns)	**(ns)	**(ns)	**(ns)
Fasting Glucose (Diabetics) (D)	ns	ns	NS	ns
Fasting Glucose (Nondiabetics) (C)	**(ns)	NS	-0.012	NS

Table 18-80. (Continued)
Summary of Group Analyses (Model 1) for Endocrine Variables
(Ranch Hands vs. Comparisons)

	ADJUSTED			
Variable	**All**	**Officer**	**Enlisted Flyer**	**Enlisted Groundcrew**
Fasting Glucose (Nondiabetics) (D)	ns	ns	ns	NS
2-Hour Postprandial Glucose (Nondiabetics) (C)	****	****	****	****
2-Hour Postprandial Glucose (Nondiabetics) (D)	**(NS)	**(NS)	**(ns)	**(NS*)
Fasting Urinary Glucose (All Participants) (D)	NS	ns	ns	NS
Fasting Urinary Glucose (Diabetics) (D)	ns	ns	ns	NS
Fasting Urinary Glucose (Nondiabetics) (D)	--	--	--	--
2-Hour Postprandial Urinary Glucose (Nondiabetics) (D)	NS	NS	ns	NS
Serum Insulin (All Participants) (C)	**(NS)	**(NS)	**(ns)	**(NS)
Serum Insulin (All Participants) (D)				
Low vs. Normal	**(ns)	**(ns)	**(NS)	**(NS)
High vs. Normal	**(ns)	**(NS)	**(ns)	**(ns)
Serum Insulin (Diabetics) (C)	NS	NS	ns	NS
Serum Insulin (Diabetics) (D)	NS	NS	ns	NS
Serum Insulin (Nondiabetics) (C)	**(ns)	**(NS)	**(ns)	**(NS)
Serum Insulin (Nondiabetics) (D)				
Low vs. Normal	**(ns)	**(ns)	**(NS)	**(NS)
High vs. Normal	**(ns)	**(ns)	**(ns)	**(ns)
Serum Glucagon (All Participants) (C)	ns	ns	-0.028	NS
Serum Glucagon (All Participants) (D)	NS	--	--	NS
Serum Glucagon (Diabetics) (C)	**(NS)	**(NS)	**(ns)	**(NS)
Serum Glucagon (Diabetics) (D)	--	--	--	--
Serum Glucagon (Nondiabetics) (C)	ns	ns	ns*	ns
Serum Glucagon (Nondiabetics) (D)	--	--	--	--
α-1-C Hemoglobin (All Participants) (C)	NS	NS	ns	NS
α-1-C Hemoglobin (All Participants (D)	NS	NS	ns	ns
α-1-C Hemoglobin (Diabetics) (C)	****	****	****	****
α-1-C Hemoglobin (Diabetics) (D)	NS	NS	ns	NS
α-1-C Hemoglobin (Nondiabetics) (C)	**(ns)	**(ns)	**(ns)	**(NS)
α-1-C Hemoglobin (Nondiabetics) (D)	ns	ns	ns	NS
Urinary Protein (Diabetics) (D)	**(ns)	**(NS)	**(NS)	**(ns)
Serum Proinsulin (Diabetics) (C)	NS	ns	NS	NS
Serum Proinsulin (Diabetics) (D)	ns	ns	ns	NS

Table 18-80. (Continued)
Summary of Group Analyses (Model 1) for Endocrine Variables
(Ranch Hands vs. Comparisons)

Variable	ADJUSTED			
	All	Officer	Enlisted Flyer	Enlisted Groundcrew
Serum C Peptide (Diabetics) (C)	NS*	NS	NS	NS*
Serum C Peptide (Diabetics) (D)	NS	NS	NS	NS
Total Testosterone (C)[a]	**(NS)	**(NS)	**(+0.038)	**(ns)
Total Testosterone (D)	**(ns)	**(ns)	**(ns)	**(ns)
Free Testosterone (C)[a]	NS	NS	NS*	NS
Free Testosterone (D)	-0.017	ns	-0.006	ns
Sex Hormone Binding Globulin (D)	-0.048	ns	ns	ns*
Total Testosterone to Sex Hormone Binding Globulin Ratio (D)	ns	ns	ns	NS
Estradiol (C)	NS	ns	NS	ns
Estradiol (D)	ns	ns	NS	NS
Luteinizing Hormone (LH) (C)	NS	NS	NS	NS
Luteinizing Hormone (LH) (D)	ns	ns	NS	NS
Follicle Stimulating Hormone (FSH) (C)	NS	NS	NS	ns
Follicle Stimulating Hormone (FSH) (D)	NS	+0.046	NS	ns

[a] Negative difference considered adverse for this variable.
C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥ 1.00 for discrete analysis or difference of means nonnegative for continuous analysis.
-: Relative risk < 1.00 for discrete analysis or difference of means negative for continuous analysis.
--: Analysis not performed due to sparse number of abnormalities.
NS or ns: Not significant ($p>0.10$).
NS* or ns*: Marginally significant ($0.05<p\leq0.10$).
**(NS) or **(ns): Group-by-covariate interaction ($0.01<p\leq0.05$); not significant when interaction is deleted; refer to Appendix N-2 for further analysis of this interaction.
**(NS*): Group-by-covariate interaction ($0.01<p\leq0.05$); marginally significant when interaction is deleted; refer to Appendix N-2 for further analysis of this interaction.
**(...): Group-by-covariate interaction ($0.01<p\leq0.05$); significant when interaction is deleted and p-value is given in parentheses; refer to Appendix N-2 for further analysis of this interaction.
**** Group-by-covariate interaction ($p\leq0.01$); refer to Appendix N-2 for further analysis of this interaction.
Note: A capital "NS" denotes a relative risk 1.00 or greater for discrete analysis or difference of means nonnegative for continuous analysis; a lower case "ns" denotes relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

Table 18-81.
Summary of Initial Dioxin Analyses (Model 2) for Endocrine Variables (Ranch Hands Only)

Variable	Unadjusted	Adjusted
Verified Medical Records		
Past Thyroid Disease (D)	NS	NS
Composite Diabetes Indicator (D)	NS	**(NS*)
Diabetic Severity (D)		
No Treatment vs. Nondiabetic	ns	NS
Diet Only vs. Nondiabetic	NS	NS
Oral Hypoglycemic vs. Nondiabetic	+0.032	+0.001
Insulin Dependent vs. Nondiabetic	ns	NS
Time to Diabetes Onset[a] (C)	NS	ns
Physical Examination		
Thyroid Gland (D)	--	--
Testicular Volume: Minimum[a] (C)	ns	**(ns*)
Testicular Volume: Total[a] (C)	ns	**(ns*)
Retinopathy Results (Diabetics) (D)	NS	--
Neuropathy Results (Diabetics) (D)	NS	NS
Radial Pulses (Doppler) (Diabetics) (D)	--	--
Femoral Pulses (Doppler) (Diabetics) (D)	ns	ns
Popliteal Pulses (Doppler) (Diabetics) (D)	ns	ns
Dorsalis Pedis Pulses (Doppler) (Diabetics) (D)	NS	NS
Posterior Tibial Pulses (Doppler) (Diabetics) (D)	ns	ns
Leg Pulses (Doppler) (Diabetics) (D)	NS	NS
Peripheral Pulses (Doppler) (Diabetics) (D)	NS	NS
Laboratory		
Thyroid Stimulating Hormone (TSH) (C)	NS	ns
Thyroid Stimulating Hormone (TSH) (D)	NS*	NS*
Thyroxine (T_4)[a] (C)	NS	ns
Thyroxine (T_4) (D)	NS	+0.028
Anti-Thyroid Antibodies (D)	ns	ns
Fasting Glucose (All Participants) (C)	NS	**(+0.003)
Fasting Glucose (All Participants) (D)	ns	NS
Fasting Glucose (Diabetics) (C)	+0.031	NS*
Fasting Glucose (Diabetics) (D)	ns	ns
Fasting Glucose (Nondiabetics) (C)	ns	**(NS)
Fasting Glucose (Nondiabetics) (D)	ns	ns

Table 18-81. (Continued)
Summary of Initial Dioxin Analyses (Model 2) for Endocrine Variables (Ranch Hands Only)

Variable	Unadjusted	Adjusted
2-Hour Postprandial Glucose (Nondiabetics) (C)	NS	+0.041
2-Hour Postprandial Glucose (Nondiabetics) (D)	NS	**(NS)
Fasting Urinary Glucose (All Participants) (D)	+0.023	+0.002
Fasting Urinary Glucose (Diabetics) (D)	+0.031	+0.009
Fasting Urinary Glucose (Nondiabetics) (D)	--	--
2-Hour Postprandial Urinary Glucose (Nondiabetics) (D)	NS*	NS*
Serum Insulin (All Participants) (C)	NS	NS
Serum Insulin (All Participants) (D)		
Low vs. Normal	ns	ns*
High vs. Normal	ns	NS
Serum Insulin (Diabetics) (C)	ns	ns
Serum Insulin (Diabetics) (D)	-0.003	**(ns*)
Serum Insulin (Nondiabetics) (C)	+0.048	+0.035
Serum Insulin (Nondiabetics) (D)		
Low vs. Normal	ns	**(ns)
High vs. Normal	NS	**(+0.047)
Serum Glucagon (All Participants) (C)	NS	**(NS)
Serum Glucagon (All Participants) (D)	ns	ns
Serum Glucagon (Diabetics) (C)	ns	ns
Serum Glucagon (Diabetics) (D)	ns	NS
Serum Glucagon (Nondiabetics) (C)	NS*	+0.041
Serum Glucagon (Nondiabetics) (D)	--	--
α-1-C Hemoglobin (All Participants) (C)	NS*	****
α-1-C Hemoglobin (All Participants) (D)	NS	**(NS)
α-1-C Hemoglobin (Diabetics) (C)	NS*	NS
α-1-C Hemoglobin (Diabetics) (D)	NS	NS
α-1-C Hemoglobin (Nondiabetics) (C)	ns	NS
α-1-C Hemoglobin (Nondiabetics) (D)	NS	NS
Urinary Protein (Diabetics) (D)	NS	NS
Serum Proinsulin (Diabetics) (C)	NS	ns
Serum Proinsulin (Diabetics) (D)	NS	NS
Serum C Peptide (Diabetics) (C)	ns	ns*
Serum C Peptide (Diabetics) (D)	ns	ns
Total Testosterone (C)[a]	NS	**(ns)

Table 18-81. (Continued)
Summary of Initial Dioxin Analyses (Model 2) for Endocrine Variables (Ranch Hands Only)

Variable	Unadjusted	Adjusted
Total Testosterone (D)	NS	**(NS)
Free Testosterone (C)[a]	NS	ns
Free Testosterone (D)	NS	NS
Sex Hormone Binding Globulin (D)	ns	ns
Total Testosterone to Sex Hormone Binding Globulin Ratio (D)	ns	NS
Estradiol (C)	NS	NS*
Estradiol (D)	NS	NS
Luteinizing Hormone (LH) (C)	-0.012	ns*
Luteinizing Hormone (LH) (D)	NS	+0.042
Follicle Stimulating Hormone (FSH) (C)	ns	ns
Follicle Stimulating Hormone (FSH) (D)	ns	NS

[a] Negative slope considered adverse for this variable.
C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥ 1.00 for discrete analysis or slope nonnegative for continuous analysis.
-: Relative risk < 1.00 for discrete analysis or slope negative for continuous analysis.
--: Analysis not performed due to sparse number of abnormalities.
NS or ns: Not significant ($p>0.10$).
NS* or ns*: Marginally significant ($0.05<p\leq0.10$).
**(NS) or **(ns): Log_2 (initial dioxin)-by-covariate interaction ($0.01<p\leq0.05$); not significant when interaction is deleted; refer to Appendix N-2 for further analysis of this interaction.
**(NS*) or **(ns*): Log_2 (initial dioxin)-by-covariate interaction ($0.01<p\leq0.05$); marginally significant when interaction is deleted; refer to Appendix N-2 for further analysis of this interaction.
**(...): Log_2 (initial dioxin)-by-covariate interaction ($0.01<p\leq0.05$); significant when interaction is deleted and p-value is given in parentheses; refer to Appendix N-2 for further analysis of this interaction.
**** Log_2 (initial dioxin)-by-covariate interaction ($p\leq0.01$); refer to Appendix N-2 for further analysis of this interaction.
Note: P-value given if $p\leq0.05$.
A capital "NS" denotes a relative risk 1.00 or greater for discrete analysis or slope nonnegative for continuous analysis; a lower case "ns" denotes relative risk less than 1.00 for discrete analysis or slope negative for continuous analysis.

Table 18-82.
Summary of Categorized Dioxin Analyses (Model 3) for Endocrine Variables (Ranch Hands vs. Comparisons)

Variable	UNADJUSTED			
	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Verified Medical Records				
Past Thyroid Gland (D)	NS	ns	ns	ns
Composite Diabetes Indicator (D)	NS	NS	NS	NS
Diabetic Severity (D)				
No Treatment vs. Nondiabetic	NS	NS	ns	NS
Diet Only vs. Nondiabetic	ns	NS	NS	NS
Oral Hypoglycemic vs. Nondiabetic	--	ns	NS*	NS
Insulin Dependent vs. Nondiabetic	NS*	NS	NS	NS
Time to Diabetes Onset[a] (C)	NS	ns	ns	ns
Physical Examination				
Thyroid Gland (D)	NS	--	ns	ns
Testicular Volume: Minimum[a] (C)	NS	ns	NS	ns
Testicular Volume: Total[a] (C)	ns	ns	ns	ns
Retinopathy Results (Diabetics) (D)	NS	ns	NS	NS
Neuropathy Results (Diabetics) (D)	NS	ns	NS	NS
Radial Pulses (Doppler) (Diabetics) (D)	NS	NS	--	NS
Femoral Pulses (Doppler) (Diabetics) (D)	NS	NS	ns	NS
Popliteal Pulses (Doppler) (Diabetics) (D)	ns	NS	NS	NS
Dorsalis Pedis Pulses (Doppler) (Diabetics) (D)	ns	ns	NS*	NS
Posterior Tibial Pulses (Doppler) (Diabetics) (D)	ns	NS	NS*	NS
Leg Pulses (Doppler) (Diabetics) (D)	ns	ns	+0.009	NS
Peripheral Pulses (Doppler) (Diabetics) (D)	NS	ns	+0.013	NS
Laboratory				
Thyroid Stimulating Hormone (TSH) (C)	NS	NS	NS	NS
Thyroid Stimulating Hormone (TSH) (D)	ns	ns	NS	NS
Thyroxine (T_4)[a] (C)	ns	NS	NS	NS
Thyroxine (T_4) (D)	ns	ns	ns	ns
Anti-Thyroid Antibodies	NS	NS*	NS	+0.048
Fasting Glucose (All Participants) (C)	NS	ns	NS	NS

Table 18-82. (Continued)
Summary of Categorized Dioxin Analyses (Model 3) for Endocrine Variables (Ranch Hands vs. Comparisons)

Variable	UNADJUSTED			
	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Fasting Glucose (All Participants) (D)	ns	NS	NS	NS
Fasting Glucose (Diabetics) (C)	ns	ns	NS	NS
Fasting Glucose (Diabetics) (D)	NS	NS	NS	NS
Fasting Glucose (Nondiabetics) (C)	NS	NS	ns	ns
Fasting Glucose (Nondiabetics) (D)	ns	NS	ns	ns
2-Hour Postprandial Glucose (Nondiabetics) (C)	ns	NS	NS	NS
2-Hour Postprandial Glucose (Nondiabetics) (D)	ns	NS	+0.031	+0.031
Fasting Urinary Glucose (All Participants) (D)	ns	ns	NS	NS
Fasting Urinary Glucose (Diabetics) (D)	ns	ns	NS	NS
Fasting Urinary Glucose (Nondiabetics) (D)	--	--	--	--
2-Hour Postprandial Urinary Glucose (D)	ns	NS	NS*	NS
Serum Insulin (All Participants) (C)	ns	NS	NS	NS
Serum Insulin (All Participants) (D)				
Low vs. Normal	ns	ns	ns	ns
High vs. Normal	ns	ns	ns	ns
Serum Insulin (Diabetics) (C)	NS	NS*	ns	NS
Serum Insulin (Diabetics) (D)	NS	NS	ns	ns
Serum Insulin (Nondiabetics) (C)	ns	ns	NS*	NS
Serum Insulin (Nondiabetics) (D)				
Low vs. Normal	ns	ns	ns	ns
High vs. Normal	-0.040	ns	NS	ns
Serum Glucagon (All Participants) (C)	ns	ns	ns	ns
Serum Glucagon (All Participants) (D)	NS	NS	--	NS
Serum Glucagon (Diabetics) (C)	NS	NS	ns	ns
Serum Glucagon (Diabetics) (D)	NS	NS	--	NS
Serum Glucagon (Nondiabetics) (C)	ns*	ns	NS	ns
Serum Glucagon (Nondiabetics) (D)	--	--	--	--
α-1-C Hemoglobin (All Participants) (C)	ns	NS	NS	NS
α-1-C Hemoglobin (All Participants) (D)	NS	NS	NS	NS

Table 18-82. (Continued)
Summary of Categorized Dioxin Analyses (Model 3) for Endocrine Variables (Ranch Hands vs. Comparisons)

Variable	UNADJUSTED			
	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
α-1-C Hemoglobin (Diabetics) (C)	ns	ns	NS*	NS
α-1-C Hemoglobin (Diabetics) (D)	NS	NS	NS	NS*
α-1-C Hemoglobin (Nondiabetics) (C)	ns	ns	ns*	ns*
α-1-C Hemoglobin (Nondiabetics) (D)	NS	ns	ns	ns
Urinary Protein (Diabetics) (D)	NS	ns	ns	ns
Serum Proinsulin (Diabetics) (C)	ns	ns	ns	ns
Serum Proinsulin (Diabetics) (D)	ns	ns	NS	NS
Serum C Peptide (Diabetics) (C)	NS	+0.017	NS	NS*
Serum C Peptide (Diabetics) (D)	ns	NS	ns	ns
Total Testosterone[a] (C)	+0.031	NS	ns	NS
Total Testosterone (D)	ns	ns	NS	ns
Free Testosterone[a] (C)	ns	NS	+0.033	NS*
Free Testosterone (D)	ns*	ns*	ns	ns
Sex Hormone Binding Globulin (D)	NS	ns	ns	ns*
Total Testosterone to Sex Hormone Binding Globulin Ratio (D)	ns	ns	NS	ns
Estradiol (C)	ns	ns	NS	NS
Estradiol (D)	ns	ns	ns	ns
Luteinizing Hormone (LH) (C)	NS	+0.006	ns	NS
Luteinizing Hormone (LH) (D)	NS	ns	ns	ns
Follicle Stimulating Hormone (FSH) (C)	NS	NS*	ns	NS
Follicle Stimulating Hormone (FSH) (D)	NS	NS	ns	NS

[a] Negative difference considered adverse for this variable.
C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥ 1.00 for discrete analysis or difference of means nonnegative for continuous analysis.
-: Relative risk < 1.00 for discrete analysis or difference of means negative for continuous analysis.
--: Analysis not performed due to sparse number of abnormalities.
NS or ns: Not significant ($p>0.10$).
NS* or ns*: Marginally significant ($0.05<p\leq0.10$).
Note: P-value given if $p\leq0.05$.
A capital "NS" denotes a relative risk 1.00 or greater for discrete analysis or difference of means nonnegative for continuous analysis; a lower case "ns" denotes relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

Table 18-82. (Continued)
Summary of Categorized Dioxin Analyses (Model 3) for Endocrine Variables (Ranch Hands vs. Comparisons)

Variable	ADJUSTED			
	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Verified Medical Records				
Past Thyroid Disease (D)	**(NS)	**(ns)	**(ns)	**(ns)
Composite Diabetes Indicator (D)	**(ns)	**(NS)	**(NS)	**(NS)
Diabetic Severity (D)				
No Treatment vs. Nondiabetic	ns	NS	NS	NS
Diet Only vs. Nondiabetic	ns	NS	NS	NS
Oral Hypoglycemic vs. Nondiabetic	--	ns	+0.033	NS
Insulin Dependent vs. Nondiabetic	NS	NS	NS	NS
Time to Diabetes Onset[a] (C)	NS	ns	ns	ns
Physical Examination				
Thyroid Gland (D)	NS	--	ns	ns
Testicular Volume: Minimum[a] (C)	NS	NS	ns	ns
Testicular Volume: Total[a] (C)	NS	NS	ns	ns
Retinopathy Results (Diabetics) (D)	NS	ns	NS	NS
Neuropathy Results (Diabetics) (D)	NS	ns	NS*	NS
Radial Pulses (Doppler) (Diabetics) (D)	--	--	--	--
Femoral Pulses (Doppler) (Diabetics) (D)	NS	NS	ns	NS
Popliteal Pulses (Doppler) (Diabetics) (D)	ns	NS	NS	NS
Dorsalis Pedis Pulses (Doppler) (Diabetics) (D)	ns	ns	+0.029	NS
Posterior Tibial Pulses (Doppler) (Diabetics) (D)	ns	NS	NS*	NS
Leg Pulses (Doppler) (Diabetics) (D)	ns	ns	+0.013	NS
Peripheral Pulses (Doppler) (Diabetics) (D)	ns	ns*	+0.017	NS
Laboratory				
Thyroid Stimulating Hormone (TSH) (C)	NS	NS	NS	NS
Thyroid Stimulating Hormone (TSH) (D)	ns	ns	NS	NS
Thyroxine (T_4)[a] (C)	NS	NS	ns	ns
Thyroxine (T_4) (D)	ns	ns	NS	ns
Anti-Thyroid Antibodies	NS	NS*	NS	+0.048

Table 18-82. (Continued)
Summary of Categorized Dioxin Analyses (Model 3) for Endocrine Variables (Ranch Hands vs. Comparisons)

	ADJUSTED			
Variable	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Fasting Glucose (All Participants) (C)	**(ns)	**(ns)	**(NS*)	**(NS)
Fasting Glucose (All Participants) (D)	ns	NS	NS	NS
Fasting Glucose (Diabetics) (C)	NS	ns	NS	ns
Fasting Glucose (Diabetics) (D)	**(NS)	**(ns)	**(NS)	**(ns)
Fasting Glucose (Nondiabetics) (C)	****	****	****	****
Fasting Glucose (Nondiabetics) (D)	ns	NS	ns	ns
2-Hour Postprandial Glucose (Nondiabetics) (C)	**(ns)	**(NS)	**(NS)	**(NS)
2-Hour Postprandial Glucose (Nondiabetics) (D)	ns	NS	+0.023	+0.040
Fasting Urinary Glucose (All Participants) (D)	**(ns)	**(ns)	**(NS)	**(NS)
Fasting Urinary Glucose (Diabetics) (D)	****	****	****	****
Fasting Urinary Glucose (Nondiabetics) (D)	--	--	--	--
2-Hour Postprandial Urinary Glucose (Nondiabetics) (D)	NS	NS	NS	NS
Serum Insulin (All Participants) (C)	****	****	****	****
Serum Insulin (All Participants) (D)				
Low vs. Normal	**(ns)	**(ns)	**(ns)	**(ns)
High vs. Normal	**(ns)	**(ns)	**(ns)	**(ns)
Serum Insulin (Diabetics) (C)	NS	+0.027	ns	NS
Serum Insulin (Diabetics) (D)	**(NS)	**(NS)	**(ns)	**(NS)
Serum Insulin (Nondiabetics) (C)	**(ns)	**(ns)	**(NS)	**(NS)
Serum Insulin (Nondiabetics) (D)				
Low vs. Normal	****	****	****	****
High vs. Normal	****	****	****	****
Serum Glucagon (All Participants) (C)	**(ns)	**(ns)	**(NS)	**(ns)
Serum Glucagon (All Participants) (D)	--	--	--	--
Serum Glucagon (Diabetics) (C)	**(NS)	**(NS)	**(ns)	**(ns)
Serum Glucagon (Diabetics) (D)	--	--	--	--
Serum Glucagon (Nondiabetics) (C)	ns*	ns	NS	ns
Serum Glucagon (Nondiabetics) (D)	--	--	--	--

Table 18-82. (Continued)
Summary of Categorized Dioxin Analyses (Model 3) for Endocrine Variables (Ranch Hands vs. Comparisons)

	ADJUSTED			
Variable	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
α-1-C Hemoglobin (All Participants) (C)	**(ns)	**(ns)	**(NS)	**(NS)
α-1-C Hemoglobin (All Participants) (D)	NS	NS	NS	NS
α-1-C Hemoglobin (Diabetics) (C)	NS	ns	NS	NS
α-1-C Hemoglobin (Diabetics) (D)	ns	NS	NS	NS
α-1-C Hemoglobin (Nondiabetics) (C)	NS	ns	ns	ns*
α-1-C Hemoglobin (Nondiabetics) (D)	NS	ns	ns	ns
Urinary Protein (Diabetics) (D)	NS	ns	ns	ns
Serum Proinsulin (Diabetics) (C)	ns	ns	NS	NS
Serum Proinsulin (Diabetics) (D)	ns	ns	ns	ns
Serum C Peptide (Diabetics) (C)	**(ns)	**(+0.008)	**(NS)	**(+0.038)
Serum C Peptide (Diabetics) (D)	****	****	****	****
Total Testosterone (C)[a]	+0.004	NS	ns*	ns
Total Testosterone (D)	**(ns)	**(ns)	**(NS)	**(ns)
Free Testosterone (C)[a]	NS	NS	ns	NS
Free Testosterone (D)	ns*	ns*	ns	ns
Sex Hormone Binding Globulin (D)	NS	ns	ns	-0.038
Total Testosterone to Sex Hormone Binding Globulin Ratio (D)	ns	ns	NS	NS
Estradiol (C)	ns	ns	NS	ns
Estradiol (D)	ns	ns	ns	ns
Luteinizing Hormone (LH) (C)	NS	+0.019	ns	NS
Luteinizing Hormone (LH) (D)	ns	ns	ns	ns
Follicle Stimulating Hormone (FSH) (C)	ns	NS	NS	NS
Follicle Stimulating Hormone (FSH) (D)	NS	NS	NS	NS

Table 18-82. (Continued)
Summary of Categorized Dioxin Analyses (Model 3) for Endocrine Variables
(Ranch Hands vs. Comparisons)

[a] Negative difference considered adverse for this variable.
C: Continuous analysis.
D: Discrete analysis.
+: Relative risk $\geq$ 1.00 for discrete analysis or difference of means nonnegative for continuous analysis.
-: Relative risk < 1.00 for discrete analysis or difference of means negative for continuous analysis.
--: Analysis not perforemd due to sparse number of abnormalities.
NS or ns: Not significant ($p>0.10$).
NS* or ns*: Marginally significant ($0.05<p\leq0.10$).
**(NS) or **(ns): Categorized dioxin-by-covariate interaction ($0.01<p\leq0.05$); not significant when interaction is deleted; refer to Appendix N-2 for further analysis of this interaction.
**(NS*): Categorized dioxin-by-covariate interaction ($0.01<p\leq0.05$); marginally significant when interaction is deleted; refer to Appendix N-2 for further analysis of this interaction.
**(...): Categorized dioxin-by-covariate interaction ($0.01<p\leq0.05$); significant when interaction is deleted and p-value is given in parentheses; refer to Appendix N-2 for further analysis of this interaction.
**** Categorized dioxin-by-covariate interaction ($p\leq0.01$); refer to Appendix N-2 for further analysis of this interaction.
Note: P-value given if $p\leq0.05$.
A capital "NS" denotes a relative risk 1.00 or greater for discrete analysis or difference of means nonnegative for continuous analysis; a lower case "ns" denotes relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

Table 18-83.
Summary of Current Dioxin Analyses (Models 4, 5, and 6) for Endocrine Variables (Ranch Hands Only)

Variable	UNADJUSTED		
	Model 4: Lipid-Adjusted Current Dioxin	Model 5: Whole-Weight Current Dioxin	Model 6: Whole-Weight Current Dioxin Adjusted for Total Lipids
Verified Medical Records			
Past Thyroid Disease (D)	ns	ns	ns
Composite Diabetes Indicator (D)	+0.005	+<0.001	+0.050
Diabetic Severity (D)			
No Treatment vs. Nondiabetic	NS	NS	NS
Diet Only vs. Nondiabetic	NS*	+0.007	+0.020
Oral Hypoglycemic vs. Nondiabetic	+<0.001	+<0.001	+<0.001
Insulin Dependent vs. Nondiabetic	ns	ns	ns*
Time to Diabetes Onset[a] (C)	-0.004	-0.001	-0.026
Physical Examination			
Thyroid Gland (D)	ns	ns	ns
Testicular Volume: Minimum[a] (C)	ns	ns	ns
Testicular Volume: Total[a] (C)	ns	ns	ns
Retinopathy Results (Diabetics) (D)	NS*	NS*	NS
Neuropathy Results (Diabetics) (D)	NS	NS	NS
Radial Pulses (Doppler) (Diabetics) (D)	ns	ns	ns
Femoral Pulses (Doppler) (Diabetics) (D)	ns	ns	ns
Popliteal Pulses (Doppler) (Diabetics) (D)	NS	NS	ns
Dorsalis Pedis Pulses (Doppler) (Diabetics) (D)	NS	NS	NS
Posterior Tibial Pulses (Doppler) (Diabetics) (D)	ns	NS	ns
Leg Pulses (Doppler) (Diabetics) (D)	NS	NS	NS
Peripheral Pulses (Doppler) (Diabetics) (D)	NS	NS	NS
Laboratory			
Thyroid Stimulating Hormone (TSH) (C)	NS	NS	NS
Thyroid Stimulating Hormone (TSH) (D)	NS	NS	NS
Thyroxine (T_4)[a] (C)	NS*	NS	NS
Thyroxine (T_4) (D)	NS	NS	NS
Anti-Thyroid Antibodies (D)	NS	NS	NS
Fasting Glucose (All Participants) (C)	+<0.001	+<0.001	+0.005
Fasting Glucose (All Participants) (D)	+0.011	+0.001	NS*

Table 18-83. (Continued)
Summary of Current Dioxin Analyses (Models 4, 5, and 6) for Endocrine Variables (Ranch Hands Only)

Variable	UNADJUSTED		
	Model 4: Lipid-Adjusted Current Dioxin	Model 5: Whole-Weight Current Dioxin	Model 6: Whole-Weight Current Dioxin Adjusted for Total Lipids
Fasting Glucose (Diabetics) (C)	+0.001	+<0.001	+0.025
Fasting Glucose (Diabetics) (D)	NS	NS	NS
Fasting Glucose (Nondiabetics) (C)	ns	NS	ns
Fasting Glucose (Nondiabetics) (D)	NS	NS	ns
2-Hour Postprandial Glucose (Nondiabetics) (C)	+<0.001	+<0.001	+0.001
2-Hour Postprandial Glucose (Nondiabetics) (D)	+0.001	+<0.001	+0.002
Fasting Urinary Glucose (All Participants) (D)	+<0.001	+<0.001	+0.001
Fasting Urinary Glucose (Diabetics) (D)	+0.005	+0.002	+0.018
Fasting Urinary Glucose (Nondiabetics) (D)	--	--	--
2-Hour Postprandial Urinary Glucose (Nondiabetics) (D)	+0.018	+0.005	NS*
Serum Insulin (All Participants) (C)	+<0.001	+<0.001	+<0.001
Serum Insulin (All Participants) (D)			
Low vs. Normal	-0.038	-0.021	-0.021
High vs. Normal	+0.016	+0.002	+0.013
Serum Insulin (Diabetics) (C)	ns	ns	ns
Serum Insulin (Diabetics) (D)	-0.008	-0.011	-0.029
Serum Insulin (Nondiabetics) (C)	+<0.001	+<0.001	+<0.001
Serum Insulin (Nondiabetics) (D)			
Low vs. Normal	ns	ns	ns*
High vs. Normal	+<0.001	+<0.001	+<0.001
Serum Glucagon (All Participants) (C)	NS*	+0.023	NS
Serum Glucagon (All Participants) (D)	ns	ns	NS
Serum Glucagon (Diabetics) (C)	ns	NS	ns
Serum Glucagon (Diabetics) (D)	ns	ns	NS
Serum Glucagon (Nondiabetics) (C)	+0.025	+0.013	+0.047
Serum Glucagon (Nondiabetics) (D)	--	--	--
α-1-C Hemoglobin (All Participants) (C)	+0.001	+<0.001	+0.042
α-1-C Hemoglobin (All Participants) (D)	NS*	+0.016	NS
α-1-C Hemoglobin (Diabetics) (C)	+0.010	+0.008	NS*
α-1-C Hemoglobin (Diabetics) (D)	NS	NS	NS

Table 18-83. (Continued)
Summary of Current Dioxin Analyses (Models 4, 5, and 6) for Endocrine Variables (Ranch Hands Only)

Variable	UNADJUSTED		
	Model 4: Lipid-Adjusted Current Dioxin	Model 5: Whole-Weight Current Dioxin	Model 6: Whole-Weight Current Dioxin Adjusted for Total Lipids
α-1-C Hemoglobin (Nondiabetics) (C)	ns	ns	ns
α-1-C Hemoglobin (Nondiabetics) (D)	ns	NS	ns
Urinary Protein (Diabetics) (D)	NS	NS	NS
Serum Proinsulin (Diabetics) (C)	NS	+0.047	NS
Serum Proinsulin (Diabetics) (D)	NS*	+0.031	NS
Serum C Peptide (Diabetics) (C)	NS	NS	NS
Serum C Peptide (Diabetics) (D)	ns	ns	NS
Total Testosterone (C)[a]	-<0.001	-<0.001	-<0.001
Total Testosterone (D)	+0.033	+0.012	NS*
Free Testosterone (C)[a]	ns	ns	ns
Free Testosterone (D)	+0.004	+0.009	+0.002
Sex Hormone Binding Globulin (D)	NS	NS	ns
Total Testosterone to Sex Hormone Binding Globulin Ratio (D)	NS	NS	NS
Estradiol (C)	NS	NS	NS
Estradiol (D)	NS	NS	NS
Luteinizing Hormone (LH) (C)	-0.035	ns*	-0.035
Luteinizing Hormone (LH) (D)	ns	ns	ns
Follicle Stimulating Hormone (FSH) (C)	ns	ns	ns
Follicle Stimulating Hormone (FSH) (D)	ns	NS	ns

[a] Negative slope considered adverse for this variable.
C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥ 1.00 for discrete analysis or slope nonnegative for continuous analysis.
-: Relative risk < 1.00 for discrete analysis or slope negative for continuous analysis.
--: Analysis not performed due to sparse number of abnormalities.
NS or ns: Not significant ($p>0.10$).
NS* or ns*: Marginally significant ($0.05<p\leq 0.10$).
Note: P-value given if $p\leq 0.05$.
A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or slope nonnegative for continuous analysis; a lower case "ns" denotes relative risk less than 1.00 for discrete analysis or slope negative for continuous analysis.

Table 18-83. (Continued)
Summary of Current Dioxin Analyses (Models 4, 5, and 6) for Endocrine Variables (Ranch Hands Only)

Variable	ADJUSTED		
	Model 4: Lipid-Adjusted Current Dioxin	Model 5: Whole-Weight Current Dioxin	Model 6: Whole-Weight Current Dioxin Adjusted for Total Lipids
Verified Medical Records			
Past Thyroid Disease (D)	**(ns)	NS	ns
Composite Diabetes Indicator (D)	+0.002	+<0.001	+0.041
Diabetic Severity (D)			
No Treatment vs. Nondiabetic	**(NS)	**(NS)	****
Diet Only vs. Nondiabetic	**(+0.007)	**(+<0.001)	****
Oral Hypoglycemic vs. Nondiabetic	**(+<0.001)	**(+<0.001)	****
Insulin Dependent vs. Nondiabetic	**(ns)	**(ns)	****
Time to Diabetes Onset[a] (C)	-0.001	-<0.001	-0.012
Physical Examination			
Thyroid Gland (D)	ns	ns	ns
Testicular Volume: Minimum[a] (C)	ns*	ns	**(ns*)
Testicular Volume: Total[a] (C)	ns*	ns	-0.039
Retinopathy Results (Diabetics) (D)	NS*	NS*	NS*
Neuropathy Results (Diabetics) (D)	NS	NS	NS
Radial Pulses (Doppler) (Diabetics) (D)	--	--	--
Femoral Pulses (Doppler) (Diabetics) (D)	ns	ns	ns
Popliteal Pulses (Doppler) (Diabetics) (D)	ns	NS	ns
Dorsalis Pedis Pulses (Doppler) (Diabetics) (D)	NS	****	****
Posterior Tibial Pulses (Doppler) (Diabetics) (D)	NS	NS	NS
Leg Pulses (Doppler) (Diabetics) (D)	NS	**(NS)	NS
Peripheral Pulses (Doppler) (Diabetics) (D)	****	NS	**(NS)
Laboratory			
Thyroid Stimulating Hormone (TSH) (C)	NS	NS*	NS
Thyroid Stimulating Hormone (TSH) (D)	NS	NS	NS
Thyroxine (T_4) (C)	ns	ns	ns
Thyroxine (T_4) (D)	+0.030	+0.025	+0.043
Anti-Thyroid Antibodies (D)	NS	NS	NS
Fasting Glucose (All Participants) (C)	+<0.001	**(+<0.001)	+0.005
Fasting Glucose (All Participants) (D)	+0.038	+0.005	NS
Fasting Glucose (Diabetics) (C)	+0.046	+0.017	NS
Fasting Glucose (Diabetics) (D)	****	****	****

Table 18-83. (Continued)
Summary of Current Dioxin Analyses (Models 4, 5, and 6) for Endocrine Variables (Ranch Hands Only)

Variable	ADJUSTED		
	Model 4: Lipid-Adjusted Current Dioxin	Model 5: Whole-Weight Current Dioxin	Model 6: Whole-Weight Current Dioxin Adjusted for Total Lipids
Fasting Glucose (Nondiabetics) (C)	NS	NS	ns
Fasting Glucose (Nondiabetics) (D)	ns	ns	ns
2-Hour Postprandial Glucose (Nondiabetics) (C)	+0.012	+0.002	+0.038
2-Hour Postprandial Glucose (Nondiabetics) (D)	**(+0.004)	**(+0.002)	**(+0.011)
Fasting Urinary Glucose (All Participants) (D)	+<0.001	**(+<0.001)	**(+<0.001)
Fasting Urinary Glucose (Diabetics) (D)	+0.010	+0.005	+0.027
Fasting Urinary Glucose (Nondiabetics) (D)	--	--	--
2-Hour Postprandial Urinary Glucose (Nondiabetics) (D)	NS*	+0.011	**(NS)
Serum Insulin (All Participants) (C).	NS*	+0.015	**(NS)
Serum Insulin (All Participants) (D)			
Low vs. Normal	**(ns)	**(ns)	ns
High vs. Normal	**(NS)	**(NS)	NS
Serum Insulin (Diabetics) (C)	ns	ns	ns
Serum Insulin (Diabetics) (D)	****	****	****
Serum Insulin (Nondiabetics) (C)	+0.025	+0.001	NS*
Serum Insulin (Nondiabetics) (D)			
Low vs. Normal	ns	ns	****
High vs. Normal	+0.005	+<0.001	****
Serum Glucagon (All Participants) (C)	****	+0.044	NS
Serum Glucagon (All Participants) (D)	ns	ns	NS
Serum Glucagon (Diabetics) (C)	NS	NS	ns
Serum Glucagon (Diabetics) (D)	ns	ns	NS
Serum Glucagon (Nondiabetics) (C)	+0.044	+0.027	NS*
Serum Glucagon (Nondiabetics) (D)	--	--	--
α-1-C Hemoglobin (All Participants) (C)	**(+0.012)	**(+0.002)	**(NS)
α-1-C Hemoglobin (All Participants) (D)	NS	**(NS*)	**(NS)
α-1-C Hemoglobin (Diabetics) (C)	NS	NS	NS
α-1-C Hemoglobin (Diabetics) (D)	NS*	+0.035	NS
α-1-C Hemoglobin (Nondiabetics) (C)	**(ns)	ns	ns
α-1-C Hemoglobin (Nondiabetics) (D)	ns	ns	ns
Urinary Protein (Diabetics) (D)	NS	NS	NS
Serum Proinsulin (Diabetics) (C)	NS	NS	ns

Table 18-83. (Continued)
Summary of Current Dioxin Analyses (Models 4, 5, and 6) for Endocrine Variables (Ranch Hands Only)

	ADJUSTED		
Variable	Model 4: Lipid-Adjusted Current Dioxin	Model 5: Whole-Weight Current Dioxin	Model 6: Whole-Weight Current Dioxin Adjusted for Total Lipids
Serum Proinsulin (Diabetics) (D)	****	****	****
Serum C Peptide (Diabetics) (C)	ns	ns	ns
Serum C Peptide (Diabetics) (D)	ns	**(ns)	**(ns)
Total Testosterone[a] (C)	****	**(-<0.001)	**(-0.021)
Total Testosterone (D)	**(NS)	NS	NS
Free Testosterone[a] (C)	ns	ns	ns
Free Testosterone (D)	NS	NS	NS
Sex Hormone Binding Globulin (D)	ns	NS	ns
Total Testosterone to Sex Hormone Binding Globulin Ratio (D)	NS	NS	NS*
Estradiol (C)	NS	NS	NS
Estradiol (D)	****	**(NS)	**(NS)
Luteinizing Hormone (LH) (C)	ns	ns	ns
Luteinizing Hormone (LH) (D)	ns	NS	ns
Follicle Stimulating Hormone (FSH) (C)	NS	NS	NS
Follicle Stimulating Hormone (FSH) (D)	NS	NS	NS

[a] Negative slope considered adverse for this variable.

C: Continuous analysis.

D: Discrete analysis.

+: Relative risk ≥ 1.00 for discrete analysis or slope nonnegative for continuous analysis.

-: Relative risk < 1.00 for discrete analysis or slope negative for continuous analysis.

--: Analysis not performed due to sparse number of abnormalities.

NS or ns: Not significant (p>0.10).

NS* or ns*: Marginally significant (0.05<p≤ 0.10).

**(NS) or **(ns): Log_2 (current dioxin + 1)-by-covariate interaction (p≤0.05); not significant when interaction is deleted; refer to Appendix N-2 for further analysis of this interaction.

**(NS*) or **(ns*): Log_2 (current dioxin + 1)-by-covariate interaction (0.01<p≤0.05); marginally significant when interaction is deleted; refer to Appendix N-2 for further analysis of this interaction.

**(...): Log_2 (current dioxin + 1)-by-covariate interaction (0.01<p≤0.05); significant when interaction is deleted and p-value given in parentheses; refer to Appendix N-2 for further analysis of this interaction.

**** Log_2 (current dioxin + 1)-by-covariate interaction (p≤0.01); refer to Appendix N-2 for a detailed description of this interaction.

Note: P-value given if p≤0.05.
A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or a nonnegative slope for continuous analysis; a lower case "ns" denotes relative risk less than 1.00 for discrete analysis or slope negative for continuous analysis.

Table 18-84.
Summary of Group-by-Covariate and Dioxin-by-Covariate Interactions from Adjusted Analyses of Endocrine Variables

Model	Variable	Covariate
1[a]	Past Thyroid Disease	Personality Type
	Retinopathy Results	Personality Type
	Fasting Glucose (Diabetics) (C)	Age
	Fasting Glucose (Nondiabetics) (C)	Occupation
	2-Hour Postprandial Glucose (Nondiabetics) (C)	Body Fat, Family History of Diabetes
	2-Hour Postprandial Glucose (Nondiabetics) (D)	Body Fat
	Serum Insulin (All) (C)	Age, Body Fat
	Serum Insulin (All) (D)	Age, Body Fat
	Serum Insulin (Nondiabetics) (C)	Body Fat
	Serum Insulin (Nondiabetics) (D)	Age, Body Fat
	Serum Glucagon (Diabetics) (C)	Body Fat, Diabetic Severity
	α-1-C Hemoglobin (Diabetics) (C)	Age
	α-1-C Hemoglobin (Nondiabetics) (C)	Body Fat
	Urinary Protein (Diabetics)	Race
	Total Testosterone (C)	Age
	Total Testosterone (D)	Race, Personality Type
2[b]	Composite Diabetes Indicator	Occupation
	Testicular Volume: Minimum	Occupation
	Testicular Volume: Total	Occupation
	Fasting Glucose (All) (C)	Occupation
	Fasting Glucose (Nondiabetics) (C)	Occupation
	2-Hour Postprandial Glucose (Nondiabetics) (D)	Race
	Serum Insulin (Diabetics) (D)	Age, Body Fat, Occupation
	Serum Insulin (Nondiabetics) (D)	Occupation
	Serum Glucagon (All) (C)	Occupation
	α-1-C Hemoglobin (All) (C)	Occupation
	α-1-C Hemoglobin (All) (D)	Occupation
	Total Testosterone (C)	Personality Type
	Total Testosterone (D)	Occupation

Table 18-84. (Continued)
Summary of Group-by-Covariate and Dioxin-by-Covariate Interactions from Adjusted Analyses of Endocrine Variables

Model	Variable	Covariate
3[c]	Past Thyroid Disease	Personality Type
	Composite Diabetes Indicator	Occupation
	Fasting Glucose (All) (C)	Occupation
	Fasting Glucose (Diabetics) (D)	Body Fat
	Fasting Glucose (Nondiabetics) (C)	Occupation
	2-Hour Postprandial Glucose (Nondiabetics) (C)	Body Fat, Family History of Diabetes
	Fasting Urinary Glucose (All)	Body Fat, Personality Type
	Fasting Urinary Glucose (Diabetics)	Body Fat
	Serum Insulin (All) (C)	Age
	Serum Insulin (All) (D)	Age, Body Fat, Occupation, Personality Type
	Serum Insulin (Diabetics) (D)	Age
	Serum Insulin (Nondiabetics) (C)	Age
	Serum Insulin (Nondiabetics) (D)	Occupation
	Serum Glucagon (All) (C)	Family History of Diabetes
	Serum Glucagon (Diabetics) (C)	Body Fat, Diabetic Severity
	α-1-C Hemoglobin (All) (C)	Body Fat
	Serum C Peptide (Diabetics) (C)	Occupation
	Serum C Peptide (Diabetics) (D)	Age
	Total Testosterone (D)	Personality Type
4[d]	Past Thyroid Disease	Personality Type
	Diabetic Severity	Occupation
	Peripheral Pulses	Family History of Heart Disease
	Fasting Glucose (Diabetics) (D)	Body Fat
	2-Hour Postprandial Glucose (Nondiabetics) (D)	Race
	Serum Insulin (All) (D)	Body Fat
	Serum Insulin (Diabetics) (D)	Body Fat
	Serum Glucagon (All) (C)	Family History of Diabetes
	α-1-C Hemoglobin (All) (C)	Body Fat
	α-1-C Hemoglobin (Nondiabetics) (C)	Race
	Serum Proinsulin (Diabetics) (D)	Occupation
	Total Testosterone (Diabetics) (C)	Occupation
	Total Testosterone (D)	Occupation
	Estradiol (D)	Occupation

Table 18-84. (Continued)
Summary of Group-by-Covariate and Dioxin-by-Covariate Interactions from Adjusted Analyses of Endocrine Variables

Model	Variable	Covariate
5[e]	Diabetic Severity	Occupation
	Dorsalis Pedis Pulses (Doppler) (Diabetics)	Lifetime Cigarette Smoking History
	Leg Pulses (Doppler) (Diabetics)	Lifetime Cigarette Smoking History
	Fasting Glucose (All) (C)	Body Fat
	Fasting Glucose (Diabetics) (D)	Body Fat
	2-Hour Postprandial Glucose (Nondiabetics) (D)	Race
	Fasting Urinary Glucose (All)	Personality Type
	Serum Insulin (All) (D)	Body Fat
	Serum Insulin (Diabetics) (D)	Body Fat
	α-1-C Hemoglobin (All) (C)	Age, Body Fat
	α-1-C Hemoglobin (All) (D)	Body Fat
	Serum Proinsulin (Diabetics) (D)	Occupation
	Serum C Peptide (Diabetics) (D)	Age, Diabetic Severity
	Total Testosterone (C)	Occupation
	Estradiol (D)	Occupation
6[f]	Diabetic Severity	Age
	Testicular Volume: Minimum	Occupation
	Dorsalis Pedis Pulses (Doppler) (Diabetics)	Lifetime Cigarette Smoking History
	Peripheral Pulses (Doppler) (Diabetics)	Family History of Heart Disease
	Fasting Glucose (Diabetics) (D)	Body Fat
	2-Hour Postprandial Glucose (Nondiabetics) (D)	Race
	Fasting Urinary Glucose (All)	Personality Type
	2-Hour Postprandial Urinary Glucose (Nondiabetics)	Occupation
	Serum Insulin (All) (C)	Body Fat
	Serum Insulin (Diabetics) (D)	Body Fat
	Serum Insulin (Nondiabetics) (D)	Age
	α-1-C Hemoglobin (All) (C)	Age, Body Fat
	α-1-C Hemoglobin (All) (D)	Body Fat
	Serum Proinsulin (Diabetics) (D)	Occupation, Diabetic Severity
	Serum C Peptide (Diabetics) (D)	Age, Diabetic Severity
	Total Testosterone (C)	Occupation
	Estradiol (D)	Occupation

C: Continuous Analysis.
D: Discrete Analysis.
[a] Group Analysis (Ranch Hands vs. Comparison).
[b] Ranch Hands—Log_2 (Initial Dioxin).
[c] Categorized Dioxin.
[d] Ranch Hands—Log_2 (Current Lipid-Adjusted Dioxin + 1).
[e] Ranch Hands—Log_2 (Current Whole-Weight Dioxin + 1).
[f] Ranch Hands—Log_2 (Current Whole-Weight Dioxin + 1), Adjusted for Total Lipids.

flyer Ranch Hands had a significantly lower mean level of fasting glucose than did Comparisons, but this result was nonsignificant in the analysis of all participants or diabetics alone (the unadjusted analysis revealed similar results). The analyses of the seven pulse variables, all group associations, were nonsignificant. In the unadjusted and adjusted analyses of all participants, mean serum glucagon levels were significantly lower in enlisted flyer Ranch Hands than for the corresponding Comparison category; however, stratifying the analysis of this contrast to diabetic and nondiabetic participants revealed only a marginally significant difference for nondiabetics. Serum C peptide exhibited a marginally significant positive effect for all participants and for enlisted groundcrew.

The analyses of the physical examination testes variables did not uncover any significant or notable findings, but analyses of the testosterone variables detected some significant results. In the unadjusted and adjusted analyses, free testosterone in its discrete form was significantly associated with group both overall and for enlisted flyers, where Ranch Hands had a smaller percentage of abnormal low measurements than Comparisons. A significant negative association with group also was seen in the analysis of sex hormone binding globulin. A significant group effect was seen in the analysis of total testosterone among enlisted flyers with a higher mean level in Ranch Hand enlisted flyers than in Comparison enlisted flyers, and low levels of testosterone are considered adverse.

While not evident in the unadjusted analysis, the adjusted analysis of follicle stimulating hormone detected a significantly higher percentage of abnormally high measurements in Ranch Hands than Comparisons for the officer stratum.

Model 2: Initial Dioxin Analysis

Few significant associations with initial dioxin were found in the Model 2 analyses of the thyroid variables. TSH and T_4 in the discrete analysis displayed marginally significant and significant associations respectively with initial dioxin.

Several significant interactions between initial dioxin and occupation were found in the adjusted analyses of the diabetes variables. All of these were in the investigations of the composite diabetes indicator, fasting glucose, serum insulin, serum glucagon, and α-1-C hemoglobin. The composite diabetes indicator was positively associated with initial dioxin and marginally significant. The continuous analyses of fasting glucose revealed significant and marginally significant positive associations with initial dioxin for all participants and diabetics respectively. While the continuous analyses of serum insulin on all participants and in diabetics led to nonsignificant results, the analysis on nondiabetics revealed a significant positive association with initial dioxin. Most adjusted results of discrete serum insulin were negative and marginally significant, although nondiabetics exhibited a significant positive association with initial dioxin for the abnormally high serum insulin category. The adjusted analysis of serum glucagon found a significant positive association with initial dioxin in nondiabetics. Other diabetic endpoints that displayed significant positive associations with initial dioxin were fasting urinary glucose and 2-hour postprandial glucose. A significant positive association between initial dioxin and diabetic severity was found in the contrast of Ranch Hands using oral hypoglycemics versus nondiabetics, but not for the other diabetic severity categories.

The analyses of the testes variables disclosed significant initial dioxin interactions involving occupation and personality type. Marginally significant associations with initial dioxin were evident from analyses of the minimum and total testicular volume endpoints with the interaction terms removed.

In the Model 2 analyses of the remaining endocrine variables, a significant negative association with initial dioxin was seen for luteinizing hormone in the unadjusted analysis, but this negative association was only marginally significant in the adjusted analysis. In the adjusted analysis of luteinizing hormone in discrete form, a significant positive association with initial dioxin was seen. A marginally significant positive association with initial dioxin was seen for estradiol measured continuously.

Model 3: Categorized Dioxin Analysis

Categorized dioxin analyses on the thyroid variables were nonsignificant except for the analysis of anti-thyroid antibodies. For this endpoint, a significantly greater percentage of low and low plus high Ranch Hands had anti-thyroid antibodies than did Comparisons.

The majority of the analyses on the diabetic endpoints for Model 3 detected significant interactions between categorized dioxin and various covariates (mainly body fat and occupation). Analogous to Model 1 results, when supplemental analysis was performed removing these interactions, significant differences between Ranch Hands and Comparisons were generally not evident. As an exception, analysis on serum C peptide detected a significantly greater mean level of serum C peptide in low and low plus high Ranch Hands than in Comparisons. Significant associations were exhibited in the adjusted analyses of discrete 2-hour postprandial glucose in high Ranch Hands and continuous serum insulin restricted to diabetic low Ranch Hands. Marginally significant negative results were seen in the continuous analyses of serum glucagon and α-1-C hemoglobin in nondiabetics. In the analysis of discrete serum insulin, associations in all participants, while nonsignificant, were negative; whereas for diabetics most were positive. Also, more negative associations with categorized dioxin were exhibited for the nondiabetic cohort in comparison to the all participant and diabetic cohorts in the analyses of α-1-C hemoglobin. A significantly higher percentage of Ranch Hands in the high dioxin category used oral hypoglycemics than Comparisons, but contrasts were not significant for the other diabetic severity categories. In the analysis of the pulse variables in diabetics, high dioxin Ranch Hands had significantly higher percentages of abnormalities than Comparisons for dorsalis pedis, leg, and peripheral pulses.

Data collected from the physical examination on the testes variables were analyzed by Model 3, but results were nonsignificant. For the majority of the analyses, the laboratory testes variables disclosed negative differences or relative risks less than one when comparing Ranch Hands and Comparisons. Of these results that were significant, most involved one of the testosterone variables. In the unadjusted analysis of mean free testosterone for high Ranch Hands versus Comparisons, a significant difference in means of 0.89 pg/ml was found, with the Comparisons having the lower mean. After adjusting for covariate information, the difference became negative and nonsignificant (-0.09 pg/ml). In the analysis of total testosterone, background Ranch Hands had a significantly higher mean level than

Comparisons, but the difference between high Ranch Hands and Comparisons was negative and only marginally significant.

Among the other endocrine variables, continuous Model 3 analyses of luteinizing hormone detected significant positive differences between low Ranch Hands and Comparisons.

Model 4, 5, and 6: Current Dioxin Analysis

Analyses investigating possible associations between the thyroid variables and current dioxin detected significant results for two of the laboratory variables. Thyroxine, although nonsignificant in the unadjusted analysis, exhibited significant positive associations with each analysis of current dioxin after covariate adjustment. Also, mean levels of thyroxine increased significantly with lipid-adjusted current dioxin in the unadjusted analysis, but adjusting for covariate information led to a nonsignificant negative association. Marginally significant results were found in the Model 5 adjusted analysis of thyroid stimulating hormone measured continuously, but results were nonsignificant in Models 4 and 6.

Current dioxin analyses on the diabetes variable led to several significant findings, most of which suggested a positive dose-response relationship with current dioxin. In the analysis of diabetic severity, the percentage of Ranch Hands using diet only or oral hypoglycemics to treat their diabetes showed significant associations with current dioxin. The association was not significant for insulin dependent Ranch Hands. Abnormality percentages for retinopathy results were marginally significantly related to current dioxin in each adjusted analysis, the relative risk being above 1.5 in each case. The number of years before the onset of diabetes decreased significantly with increasing levels of current dioxin for all three current dioxin analyses. All participants and diabetics generally possessed fasting glucose measurements that were positively associated with current dioxin, whereas nondiabetics alone exhibited no significant relationships for this endpoint. Similar results were seen for fasting urinary glucose. Highly significant results indicating a positive relationship with all current dioxin measurements were seen in the analyses of 2-hour postprandial glucose; however, for 2-hour postprandial urinary glucose, significant associations were apparent for whole-weight current dioxin only. The analyses of serum insulin yielded several noteworthy findings. For all participants, unadjusted analyses on this endpoint revealed highly significant results that became nonsignificant after adjusting for covariates. This was the case for the both the continuous and trichotomous discrete analyses. Inverse, albeit nonsignificant, associations with current dioxin were evident in the continuous diabetic analyses of serum insulin, whereas for all participants and nondiabetics, serum insulin increased with current dioxin (significantly so for nondiabetics). In the discrete analysis of serum insulin, associations with current dioxin were positive for the high serum insulin category and negative for the low category and were significant only for nondiabetics in Models 4 and 5. The discrete diabetic analyses of serum insulin revealed highly significant dioxin interactions with body fat. Results from analyses on serum glucagon found significant relationships only in the continuous analyses for nondiabetics, where serum glucagon increased with current dioxin. In the adjusted analyses of α-1-C hemoglobin, significant positive relationships with lipid-adjusted and whole-weight current dioxin were evident for all participants (using continuously measured α-1-C hemoglobin) and diabetics (in the discrete analysis). A noteworthy result from the α-1-C hemoglobin analyses was the prevalence of only inverse current dioxin relationships for the

nondiabetic cohort in contrast to only positive associations for diabetics. In the adjusted analyses of the diabetic variables, current dioxin interactions involving body fat and occupation comprised the majority of the significant interaction terms.

Analyses of testes variables from the physical examination revealed negative results, indicating testicular volumes decrease as current dioxin increases. Associations were marginally significant for all Model 4 and 6 analyses except for the Model 6 total testicular volume analysis, where the relationship was significant. All Model 5 analyses were nonsignificant. Notable in the total testosterone analyses from the laboratory examination was the differences between the unadjusted and adjusted analyses. All associations were significant in the continuous and discrete unadjusted analyses, but after adjusting for covariates, only the Model 5 and 6 continuous analyses revealed significant results. Also, the continuous analyses yielded results indicative of a negative dose-response relationship. Similar to the continuous analyses, the discrete analyses disclosed associations of a positive nature indicating an increase in abnormally low testosterone as dioxin increased. Unadjusted continuous analyses of free testosterone led to significant results for Models 4, 5, and 6. After covariate adjustment, however, all of these analyses were nonsignificant. Analyses on the sex hormone binding globulin variables yielded primarily nonsignificant results.

In the remaining current dioxin analyses of the endocrine variables, significant negative associations were seen for luteinizing hormone in the unadjusted analysis but were nonsignificant after adjusting for covariate information.

CONCLUSION

The assessment of the endocrine system yielded an extensive evaluation of thyroid, pancreatic, and gonadal functions and their relation to dioxin exposure. Analyses of thyroid functions did not identify significant differences between Ranch Hands and Comparisons. Similarly, the prevalence of diabetes mellitus in the two populations was not significantly different, although significant positive associations were found between current dioxin levels and the onset of diabetes.

Significant glucose metabolism results were confined to the current serum dioxin analyses. These results suggest a possible mechanism for dioxin effect on glucose metabolism and the development of diabetes. Ranch Hands with high levels of current serum dioxin had significantly higher fasting glucose levels than those with lower levels of dioxin, a result due mainly to the diabetic cohort. Nondiabetics, on the other hand, exhibited an inverse association between fasting glucose and current serum dioxin and a positive association between 2-hour postprandial glucose and current serum dioxin. Serum dioxin levels were significantly related to elevated insulin levels in nondiabetics, but not in diabetics. This is suggestive of a TCDD effect on glucose metabolism with a heightened release of insulin in Ranch Hands with a fully responsive pancreas. When this pancreatic response is no longer effective, elevated glucose levels lead to the clinical diagnosis of diabetes mellitus and loss of the dose-response between TCDD and insulin.

Analyses of gonadal functions detected a significant inverse dose-response relationship between current serum dioxin and total serum testosterone in Ranch Hands. These results

support those described in the Serum Dioxin Analysis of the 1987 Followup Examination, but the clinical significance is uncertain.

In conclusion, though the existence of endocrine disorders is comparable in Ranch Hands and Comparisons, the assessment of glucose metabolism shows the possibility of detrimental effects from dioxin in relation to glucose intolerance and insulin production.

CHAPTER 18
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